MEDICAL MICROBIOLOGY TESTING IN PRIMARY CARE

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DISCLAIMER

This book is written as a general education text in microbiology for primary care physicians and nurses. In this setting, the organisms, clinical scenarios, and diagnostic methods discussed relate to more common circumstances. In clinical practice, other organisms need to be considered. Diagnostic tests used must be agreed with the local laboratory, and specimen collection done according to the manufacturer's guidelines.

The information on the susceptibility of organisms to a particular antibiotic represents the more usual and general sensitive/resistant profile of the particular organism, and variations must take into account local, regional, and national trends. In clinical practice, reference must be made to national documents such as the British National Formulary and locally agreed antibiotic guidelines, where dosages, frequency administration, contradictions, interactions, and cautions are identified. A draft set of antibiotic guidelines is included, as an example of a document that can be used in primary care. This can be the basis for guidelines in the community, which should then be agreed by all concerned groups locally before use in clinical practice.

The authors name specific antimicrobial agents as educational examples within a particular class, where other agents can also be used appropriately. The statement in this paragraph also applies to vaccination, vaccines, and diagnostic tests and specimen collection systems.

PREFACE

Our book differs in various ways from standard texts in medical microbiology, as its main purpose is to approach the subject by addressing the needs of primary care physicians, nurses, and medical microbiology staff, and how these needs relate to each other.

While the day-to-day problems of diagnosis and treatment apply equally in primary care and in hospital medicine, doctors and nurses in primary care are separated from the on-site microbiology services available in hospitals. There is inevitably less frequent contact between the primary care physician and the laboratory and, when there is, it often addresses a specific problem involving a single patient. Yet these issues and problems are recurrent, and in our opinion a more comprehensive and systematic approach would help deal more effectively with them.

Not infrequently, for example, a specimen is taken without good reason, initiating a chain of events that can end with the patient being given an antibiotic for no clinical reason. This may not only be unsafe; it is also a waste of resources.

The key to using the laboratory effectively is to employ three basic principles:

- *Is there a valid clinical reason for taking the specimen?*
- *What is the quality of the specimen, and has the patient been given clear instructions on specimen collection?*
- *How is the laboratory report interpreted?*

These principles require an understanding of the fundamental difference between, for example, bacteria colonizing a site such as a chronic leg ulcer, and their ability to cause infection.

Our book is structured to help put these principles into practice. Each chapter opens with a scenario to identify key steps in processing a particular specimen type. In Chapters 3–10, these are followed by Quick Action Guides which, together with the information in the scenarios, can be used as a template for meetings to assess current practice and implement changes (protocols) where appropriate. As part of this, guidelines produced by the UK's Health Protection Agency (HPA) and National Institute for Clinical Excellence (NICE) have been adapted in the Quick Action Guides.

The key chapters, accounting for more than 80% of the bacteriology specimens submitted by primary care practices, are the urine specimen (Chapter 3), the genital specimen (Chapter 4), and the swab of the chronic leg ulcer (Chapter 5). If all primary care services could develop and maintain a high standard for these specimens, this would immediately bring about a significant improvement in patient care. The full benefit will be realized when primary care services and the local laboratory work together to ensure all the critical steps outlined in the scenarios are effectively managed.

The fundamental purpose of our book is to help improve patient care. We hope that adherence to its precepts may also bring economic benefits to primary care and to microbiology laboratory services.

ABBREVIATIONS

AECB	acute exacerbation of chronic bronchitis
AFB	acid fast bacilli
ALF	acute liver failure
ALO	actinomyces-like organisms
ANC	antenatal clinic
AOM	acute otitis media
ARF	acute renal failure
BAL	broncho-alveolar lavage
BBV	blood-borne virus
BCG	bacillus Calmette–Guérin
BNF	*British National Formulary*
BV	bacterial vaginosis
CA-MRSA	community-associated MRSA
CAP	community-acquired pneumonia
CDAD	*Clostridium difficile*-associated diarrhoea
CDC	Centres for Disease Control (and Prevention)
CDT	*Clostridium difficile* toxin
CFT	complement fixation test
CNS	coagulase-negative staphylococcus
COPD	chronic obstructive pulmonary disease
CRP	C-reactive protein
CSD	cat-scratch disease
CSU	catheter specimen urine
CVS	congenital varicella syndrome
DBP	diastolic blood pressure
DNA	deoxyribonucleic acid
DTB	*Drug and Therapeutics Bulletin*

EBNA	Epstein–Barr nuclear antigen
EBV	Epstein–Barr virus
ECS	endocervical swab
EDTA	ethylenediamine tetra acetic acid
EHD	environmental health department
EHO	environmental health officer
EIA	enzyme immunoassay
EM	erythema migrans
EMU	early morning urine
ENT	ear, nose, and throat
EPP	exposure-prone procedure
ESBL	extended-spectrum β-lactamase
ET	epidermolytic toxin
FBC	full blood count
FCU	first-catch urine
F/O	faecal/oral
GAS	group A streptococcus
GBS	group B streptococcus
GCS	group C streptococcus
GDH	glutamate dehydrogenase
GGS	group G streptococcus
GIT	gastrointestinal tract
GRE	glycopeptide-resistant enterococci
GU	gonococcal urethritis
HAV	hepatitis A virus
HBIG	hepatitis B virus immunoglobulin
HBcAb	HBV core antibody
HBeAg	HBV e antigen
HBsAb	HBV surface antibody
HBsAg	HBV surface antigen
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCP	health-care professional
HCV	hepatitis C virus
HCW	health-care worker
HEV	hepatitis E virus
HIV	human immunodeficiency virus
HNIG	human normal immunoglobulin
HPA	Health Protection Agency
HPU	health protection unit
HPV	human papilloma virus
HSV	herpes simplex virus
HUS	haemolytic uraemic syndrome
HVS	high vaginal swab
IDU	intravenous drug use/user
IGT	interferon gamma test
IM	infectious mononucleosis
IUCD	intrauterine contraceptive device
IUGR	intrauterine growth retardation
KOH	potassium hydroxide
MALT	mucosa-associated lymphoid tissue
MC&S	microscopy, culture, and sensitivity
MDR-TB	multidrug-resistant *Mycobacterium tuberculosis*
MOTT	mycobacteria other than tuberculosis
MSM	men who have sex with men
MSSA	methicillin-sensitive *Staphylococcus aureus*
MSU	mid-stream urine
MRSA	methicillin-resistant *Staphylococcus aureus*
NAAT	nucleic acid amplification test
NGU	nongonococcal urethritis
NICE	National Institute for Clinical Excellence
NSAID	nonsteroidal anti-inflammatory drug
OCP	ova, cysts, parasites
OHD	occupational health department
ORS	oral rehydration salts
OPAT	outpatient parental antibiotic therapy
PBP	penicillin-binding protein
PCR	polymerase chain reaction
PID	pelvic inflammatory disease
PPI	proton-pump inhibitor
PT	pertussis toxin
PVL	Panton–Valentine leukocidin
RBC	red blood cell
RNA	ribonucleic acid
RPR	rapid plasma reagin
RSV	respiratory syncitial virus
RTI	respiratory tract infection
RT-PCR	reverse transcriptase PCR
RUQ	right upper quadrant
SARS	severe acute respiratory syndrome
SBP	systolic blood pressure
SOP	standard operating procedure
SS	single stranded
SSSS	staphylococcal scalded skin syndrome
STD	sexually transmitted disease
STEC	shiga toxin-producing *Escherichia coli*
STI	sexually transmitted infection
TAT	turnaround time
TB	tuberculosis
TKR	total knee replacement
TPPA	*Treponema pallidum* particle agglutination
TSS	toxic shock syndrome
TST	tuberculin skin test
TV	*Trichomonas vaginalis*
VHF	viral haemorrhagic fever
URTI	upper respiratory tract infection
US	urethral swab
UTI	urinary tract infection
VCA	virus capsid antigen
VDRL	venereal disease research laboratory
VHF	viral haemorrhagic fever
VISA	vancomycin-intermediate *Staphylococcus aureus*
VRSA	vancomycin-resistant *Staphylococcus aureus*
VTM	viral transport medium
VVS	vulvo-vaginal swab
VZIG	varicella zoster immunoglobulin
VZV	varicella zoster virus
WCC	white cell count
ZN	Ziehl–Neelsen

1 The Introduction

- Introduction
- Critical steps
- Assessing one's own microbiology knowledge
- The laboratory repertoire
- Specimen collection
- The request form
- The role of the laboratory
- Epidemiology of specimens received from primary care
- Public health and the community
- Notification of infectious diseases and causative agents
- Summary and key points

INTRODUCTION

The complexity of medicine has changed significantly in recent years. This makes it difficult for those, both in training and in practice, to maintain the breadth of knowledge sufficient always to deal effectively with patients presenting with conditions spanning all the disciplines. Medical microbiology is no exception. While most doctors in the developed world have unrestricted access to the laboratory and the diverse range of tests available, knowing how to use these facilities and interpret laboratory results is a prerequisite for ensuring good quality, safe and cost-effective patient care.

Incorrect use of the laboratory and misinterpretation of a report wastes money and can compromise patient care, but how often does this actually occur? Is this occasionally, weekly, or daily? Practising microbiologists would state that this situation arises frequently both in primary care and the hospital setting across the strata of grades of experience. As evidence, when 130 primary care physicians were asked to interpret reports based on situations they would regularly encounter, their responses resulted in incorrect management in over 50% of cases. The purpose of this book is not to teach medical microbiology. It is to provide an understanding of the essential principles which are applicable at key steps in the process, from considering whether to take a specimen through to interpreting the result.

A report of a wound swab is shown below:

JJ		Age 76 years
Specimen:	Wound swab	
Clinical details:	Chronic venous leg ulcer; sloughy	
Result:	Profuse growth of *Staphylococcus aureus*	
	Flucloxacillin	S
	Erythromycin	S

The swab may have been requested by yourself, but not uncommonly it may have been collected by a practice/clinic partner or nurse, or taken in hospital. You are now being asked by the nurse to prescribe antibiotics; what do you do? One's natural instinct may be to prescribe flucloxacillin or erythromycin; however, is this the correct action to take? Frequently this is not the case. The key to interpreting any report is knowledge and implementation of a few essential principles. Too often a laboratory report listing an organism and its antibiotic susceptibility profile is seen as a directive to start treatment. Why would this be incorrect? Although *Staphylococcus aureus* is the major cause of wound/soft tissue infections, it can 'colonize' an ulcer or wound (i.e. it is present on the surface of the wound but not causing any harm). In such a situation antibiotic therapy is not warranted. However, if there is evidence of infection, for example cellulitis around the ulcer, an antibiotic would be indicated.

When reviewing a laboratory report, the reason for the specimen being collected should be checked; was it taken because there was clinical evidence of infection? If there was and a recognized pathogen identified, then the treatment decision would be straightforward. Frequently however, leg ulcers are swabbed as a matter of 'routine' irrespective of whether there is infection or not. Once taken, a chain of events is initiated that not only wastes resources, but which can ultimately result in patient harm. The points below highlight key consequences of inappropriate specimen collection:

- The financial cost of the unnecessary specimen.
- The financial cost of inappropriate antibiotic prescription.
- The side-effects associated with antibiotic use.
- The selection of antibiotic-resistant bacteria.
- The risk of the patient acquiring *Clostridium difficile*-associated diarrhoea (CDAD). The risk of this potentially life-threatening infection must always be considered.
- The risk of 'medicalizing' the condition, with patient expectation that an antibiotic should be given.

CRITICAL STEPS

Central to this book is the identification of seven critical steps from deciding why to take the specimen through to interpreting the laboratory report. A scenario is given at the beginning of Chapters 3–10. The purpose of these is to highlight steps which have a major bearing (critical control point) on the outcome of a consultation, should a laboratory test be ordered.

While several of the critical steps (4–6) are the responsibility of transport logistics and the laboratory, steps 1, 2, 3, and 7 have been identified to facilitate improvement in patient care, which can be used by health-care workers (HCW) as an audit and educational tool within the primary care setting.

For example, critical step 1 centres on criteria that should be used when considering collecting a specimen. In the example given in **1**, page 11, what

should prompt taking a swab from a leg ulcer? This can lead to an interesting discussion, as the reasons for swabbing may be highly varied, and the process should be educational. The endpoint should be to agree a protocol for when to take a swab. Unless screening for an organism such as methicillin-resistant *Staphylococcus aureus* (MRSA), the specimen should be collected only when there is clinical evidence of infection. By using steps 1, 2, 3, and 7 it should be possible to reduce the number of unnecessary specimens collected and the inappropriate treatment of patients, which will result in financial savings.

ASSESSING ONE'S OWN MICROBIOLOGY KNOWLEDGE

With reference to the survey of 130 primary care physicians cited above, they were presented with 12 common laboratory reports and were asked how they would manage each situation. Over 50% of the responses would have resulted in incorrect management. These scenarios plus eight others are presented in the appendix of this chapter as questions and answers, and we recommend that you do this exercise, which sets the theme for the book. As a minimum, appreciating and applying the basic principles arising from these 20 scenarios, which are encountered frequently, would improve medical practice. Even if the individual scores well, it is likely that other staff members would benefit from the quiz.

THE LABORATORY REPERTOIRE

Primary care submits a wide range of specimen types to the medical microbiology laboratory (**2**, page 12).[1, 2] For bacteriology, culture on agar plates is the main method used to isolate, identify bacteria, and determine their antibiotic susceptibility profile. Mycology includes microscopy and culture for dermatophytes in skin scrapings, nail clippings, and scalp hairs. Virology is the domain of the wide range of serological tests for antigens of, and antibodies to, most medically important viruses. In addition, antibody tests for bacteria such as treponema and leptospira are conducted in the virology section. Growing viruses in tissue culture for identification has largely been superseded by nucleic acid amplification tests (NAAT) such as the polymerase chain reaction (PCR). PCR tests are available for chlamydia and most viruses including herpes simplex virus (HSV), varicella zoster virus (VZV), and mumps. In addition, it is available for a range of respiratory pathogens including mycoplasma, influenza, and respiratory syncitial virus (RSV). PCR is integral in the management of antiviral regimes used in patients infected with human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV).

The 2009 H1N1 swine flu pandemic identified the challenges, in the UK at least, of introducing a new PCR-based diagnostic test for use in both the community and hospital setting. The availability of PCR tests in microbiology and virology should be confirmed with the local laboratory.

SPECIMEN COLLECTION

Highlighted in the first figure of each of Chapters 3–10 are key points in the collection and storage of the various types of specimen. These points are emphasized in more detail in each chapter, and the accompanying Quick Action Guide. Critical step 2 also covers this in detail. Staff needs to know how to collect a good quality specimen. Where patients are expected to collect their own specimen, they need to be given appropriate advice on how to do so. Failure to give this advice can invalidate the whole process. One example is the female patient not being given practical advice on how to collect a urine specimen at home (see Chapter 3, **45**, **46**).

THE REQUEST FORM

To ensure that the correct tests are done, the request form accompanying the specimen should include comments on the clinical situation, relevant travel and occupational details, antibiotic allergies, as well as current and proposed antibiotic use. Further tests may be done on the basis of this information. The laboratory is responsible for providing useful information on the report that can be used directly to manage the patient. Examples of the details that should be recorded on request forms and laboratory reports are shown in **3**, page 13. It is essential that the full details of the patient, as well as those of the requesting Practice and practitioner are clearly entered on the request form. Failure to do so leads to errors at data entry in the laboratory, and may delay or prevent the final report from reaching its destination.

THE ROLE OF THE LABORATORY

The primary care physician should involve the medical microbiologist/infectious diseases physician in relevant management decisions at appropriate stages of the process. A readily accessible consultant-led medical microbiology service is thus good customer and patient care. As shown in **4**, page 14, this not only includes routine advice, but a prompt service when an 'urgent' clinical situation arises.

However, the medical microbiologist/infectious diseases physician is not in a position to give advice on every report.

Pathology laboratory services are regulated by national accreditation bodies. In the UK, the organization is Clinical Pathology Accreditation (UK) Ltd. This organization sets standards for all aspects of the service, including standard operating procedures (SOPs) for processing specimens from receipt to final report, audit, quality control, safety, plus professional development and training of staff. Laboratories are inspected on a regular basis to check compliance with the standards.

One important topic is the turnaround time (TAT) from specimen collection to reporting. Laboratories vary in the times that they are open for routine service. Many have adopted or are working towards an extended day, working 7 days a week. Laboratories that do not have a full weekend service can provide good TATs during the week, but this will be extended for specimens collected at the end of the week, when work is completed on the following Monday. Delays in storage can lead to deterioration of the quality of the specimen, which produces an unhelpful report, which may generate the need for collecting a repeat specimen. As with all health-care services, laboratories are under financial pressure to save money and one key area is control of workload. Thus removing unnecessary tests from the system will enable the laboratory to target its resources to improve TATs by providing the service 7 days a week (i.e. specimens sent late on a Friday will now have a result on a Monday morning). This will improve the quality of critical steps 3–6, which again improves patient care. It is thus essential that users, including primary care, work closely with the laboratory to integrate the quality of the service in all the critical steps 1–7 (**1**).

1 Critical steps in the decision process for taking and handling of specimens of the chronic leg ulcer. This is an example of the potential consequence of taking a specimen when there is no clinical indication, and the subsequent misinterpretation of the report. The steps in the process can be divided into seven critical steps. Similar examples are given at the beginning of chapters 3–10, and can be used as a teaching tool for staff to review the methods used at each relevant step, and agree protocols for uniform best practice. (Steps 4–6 are the critical steps in logistics and the laboratory process that should be part of the overall quality management system.)

Critical step 1: Is collection of a specimen indicated? Is there clinical evidence of infection? With the chronic leg ulcer, there are both local and systemic signs of infection that should be used in assessing the ulcer and the patient. With the chronic leg ulcer it is very important to differentiate colonization/critical colonization from infection. '+++ slough' is not a sign of infection. (See Chapter 5.)

Critical step 2: Obtain a good quality specimen. A swab should be collected from a site where there is evidence of infection. Ulcers will always be colonized by bacteria. Those growing on the superficial layer or slough will often not represent the pathogen causing the infection adjacent to viable tissue.

Critical step 3: Record the full patient and clinical details and type of specimen on the request form. Where necessary, record the specific test request. Full patient details are essential in determining the quality of data entry in the laboratory, and thus the accuracy of ongoing records of a patient. In this example, 'MC & S' is sufficient for the test request. (In other situations, for example examination of a sputum for tuberculosis, 'AFB/TB culture' must be entered on the request form.)

CRITICAL STEP 4: How is the specimen stored and what is the frequency of transport to the laboratory? In each chapter, details of specimen collection are outlined in the first figure, and the text of that chapter. Primary care practices/clinics will have a designated refrigerator for specimen storage, which should have some form of temperature monitoring.

CRITICAL STEPS 5 AND 6 are the responsibility of the logistics/transport service and the laboratory, and standard operating procedures will be in place. The laboratory must have set procedures for communicating 'urgent' results to primary care staff.

Critical step 7: Interpretation of the laboratory report.

This involved several steps with this scenario:

1. Ascertain if there was clinical evidence of infection. If not, the report can be ignored in most circumstances (exception is a MRSA screening result).
2. If there is clinical evidence of infection, is the organism reported likely to be causing the infection? If the answer is yes, confirm that the antibiotic prescription is correct. If the organism is unlikely to be causing the infection, or a resistant organism such as MRSA is reported, review the patient to determine the response to any treatment that has been given, and then consider further management.

The outcome of this scenario, which started with a specimen being taken for no good clinical reason, was the unnecessary prescription of ciprofloxacin given as treatment for the pseudomonas, an uncommon cause of infection in chronic leg ulcers. The antibiotic resulted in the patient developing *Clostridium difficile*-associated diarrhoea (CDAD).

1

CRITICAL STEP 1:
Is collection of a specimen indicated?

Primary care team incorrectly decides to collect a swab from a leg ulcer of a 75-year-old patient, as it has ' +++ slough'.

CRITICAL STEP 2:
Obtain a good quality specimen.

Practice nurse collects swab of superficial layer of ulcer.

CRITICAL STEP 3:

Record the full patient and clinical details and type of specimen on the request form. Where necessary, record the specific test request.

CRITICAL STEP 4:

How is the specimen stored and what is the frequency of transport to the laboratory?

CRITICAL STEP 5:

What is the quality of the laboratory process, including turnaround times?

CRITICAL STEP 6:

Is immediate or routine reporting of this result required by the laboratory?

CRITICAL STEP 7:
Interpretation of the laboratory report.

Report on AB, 75-year old. Leg ulcer MC&S:

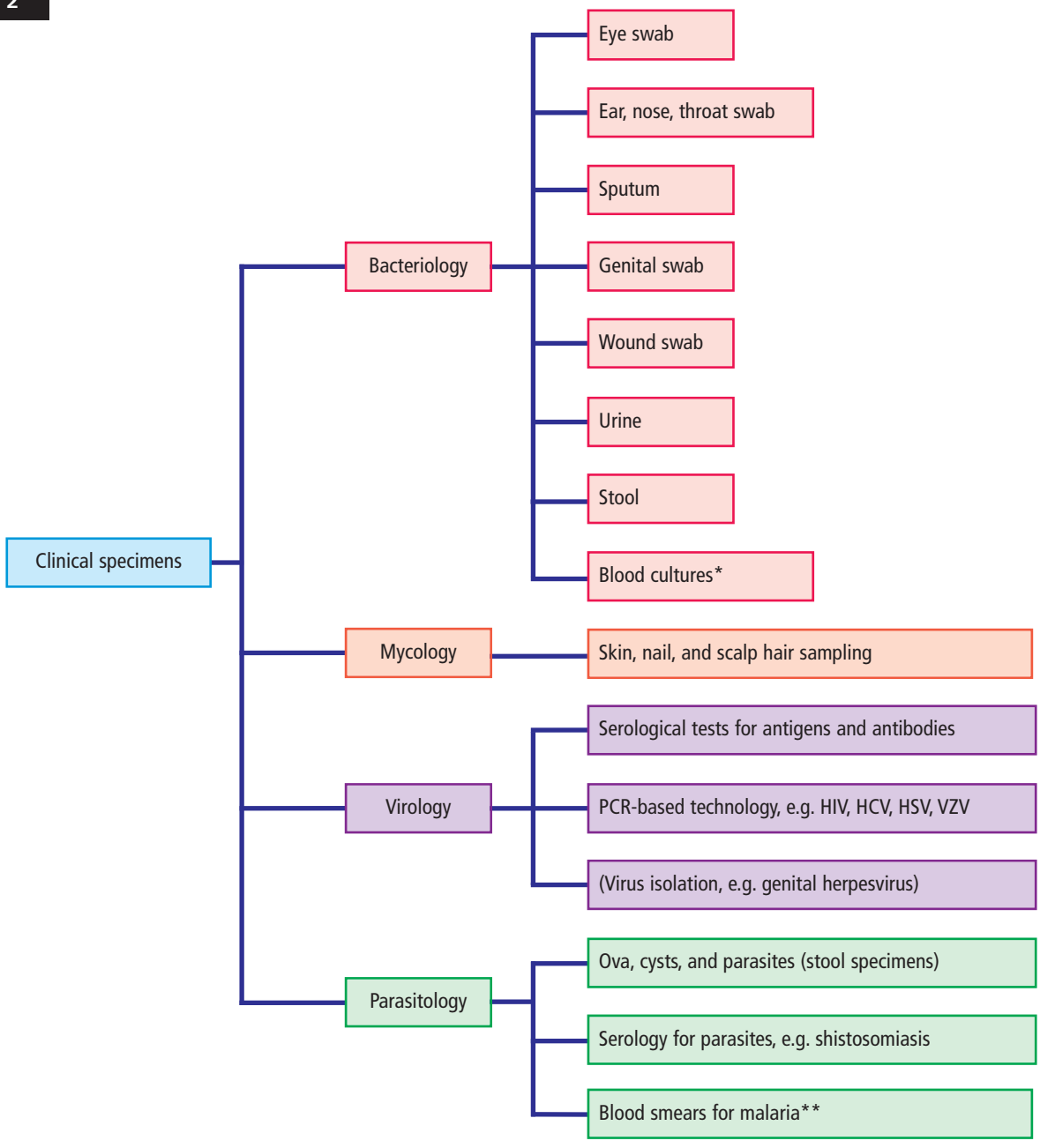
Profuse growth of *Pseudomonas aeruginosa*

(Antibiotic susceptibilities done, but results are not released on the report).

On reviewing the result, and assuming that pseudomonas is usually ciprofloxacin sensitive, the primary care physician prescribes: Ciprofloxacin 500 mg q12h for 7 days.

5 days after completing the course of ciprofloxacin, the patient develops diarrhoea, confirmed as *Clostridium difficile*-associated diarrhoea, and requires hospital admission.

2



*Blood cultures are not often collected in primary care, and cases where this is being considered should be discussed with the medical microbiologist/infectious diseases physician.
**Blood smears for malaria (in an EDTA containing tube) need to be examined within 3 hours of collection. This is usually the domain of the haematology department.

2 The medical microbiology laboratory processes a wide range of specimen types from primary care. Serology is the domain of the virology section, and includes antibody (and certain antigen) tests for viruses, bacteria, fungi, and protozoa. The isolation of viruses in cell culture is largely being replaced by more rapid and sensitive molecular tests such as the PCR.

3

(a)

Patient's name and address: Date of birth:	National health or hospital number:
Primary care practice/clinic and/or code:	Date of collection:
Primary care physician: name and initials:	Phone number:
Specimen type:	Test required:
Clinical details: Including symptoms/signs, date of exposure (where relevant), occupation, travel history, proposed, current or recent antibiotics, antibiotic allergies, other (e.g. pregnancy).	

(b)

Patient's name and address: Date of birth:	National health or hospital number:
Primary care practice/clinic and/or code:	Date of collection:
Primary care physician: name and initials:	Phone number of laboratory:
Specimen type:	Test done:
Clinical details: Including occupation, travel. Proposed, current, or recent antibiotics. THE LABORATORY REPORT SHOULD LIST: • THE ORGANISM(S) ISOLATED AND IDENTIFIED • USEFUL ANTIBIOTIC SUSCEPTIBILITY RESULTS • USEFUL INTERPRETIVE COMMENT	

Date of receipt in the laboratory	Date of authorization	Name of person authorizing report

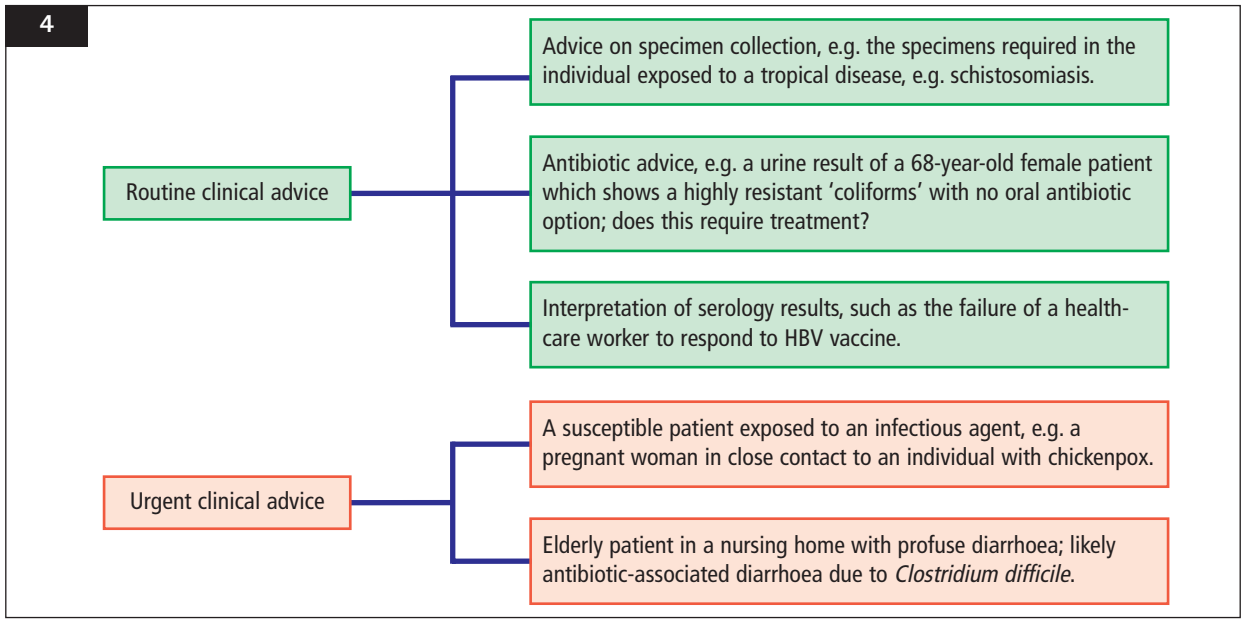
3 Important information to be included on **(a)** the request form by the requestor, and **(b)** the report form by the laboratory. Incomplete details create problems with accuracy at data entry, and can also result in multiple entries for one individual on the laboratory information technology system.

This includes how results are communicated to the primary care practice/clinic, which are urgent, which are routine, and what information should be recorded on the report. It is recognized that microbiology reports are often misinterpreted, which leads to inappropriate antibiotic prescribing.[3, 4]

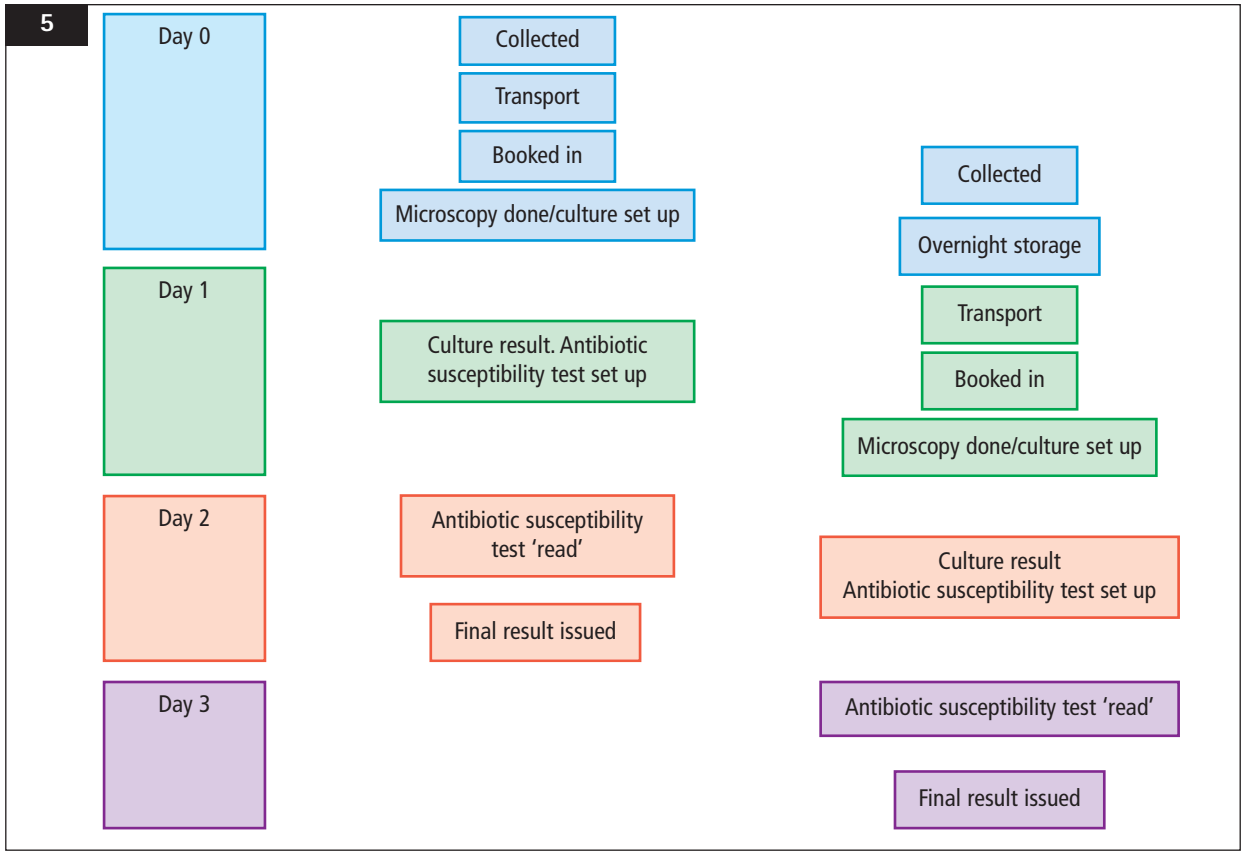
The transport logistics that are in place to cover the wide geographical area which a typical laboratory serves is also key. An example of how a delay in specimen receipt in the laboratory affects TAT is shown in **5**, page 14.

EPIDEMIOLOGY OF SPECIMENS RECEIVED FROM PRIMARY CARE

Bacteriology specimens sent to the medical microbiology laboratory include urines, genital and wound swabs, and stools. Examination of the total number of bacteriology specimens submitted during 2 weeks (1 week in October 2008 and 1 in April


4
Routine clinical advice
Advice on specimen collection, e.g. the specimens required in the individual exposed to a tropical disease, e.g. schistosomiasis.
Antibiotic advice, e.g. a urine result of a 68-year-old female patient which shows a highly resistant 'coliforms' with no oral antibiotic option; does this require treatment?
Interpretation of serology results, such as the failure of a health-care worker to respond to HBV vaccine.
Urgent clinical advice
A susceptible patient exposed to an infectious agent, e.g. a pregnant woman in close contact to an individual with chickenpox.
Elderly patient in a nursing home with profuse diarrhoea; likely antibiotic-associated diarrhoea due to Clostridium difficile.

4 Clinical advice should be readily available from the laboratory. Complete clinical details on the request form are the basis for good communication. There should be local agreements in place relating to the antibiotics tested and reported by the laboratory, which then determine antibiotic guidelines in the community. Ideally, there should be a forum for microbiology (pathology) to interface directly with primary care to ensure better communication and ultimately improved patient care.

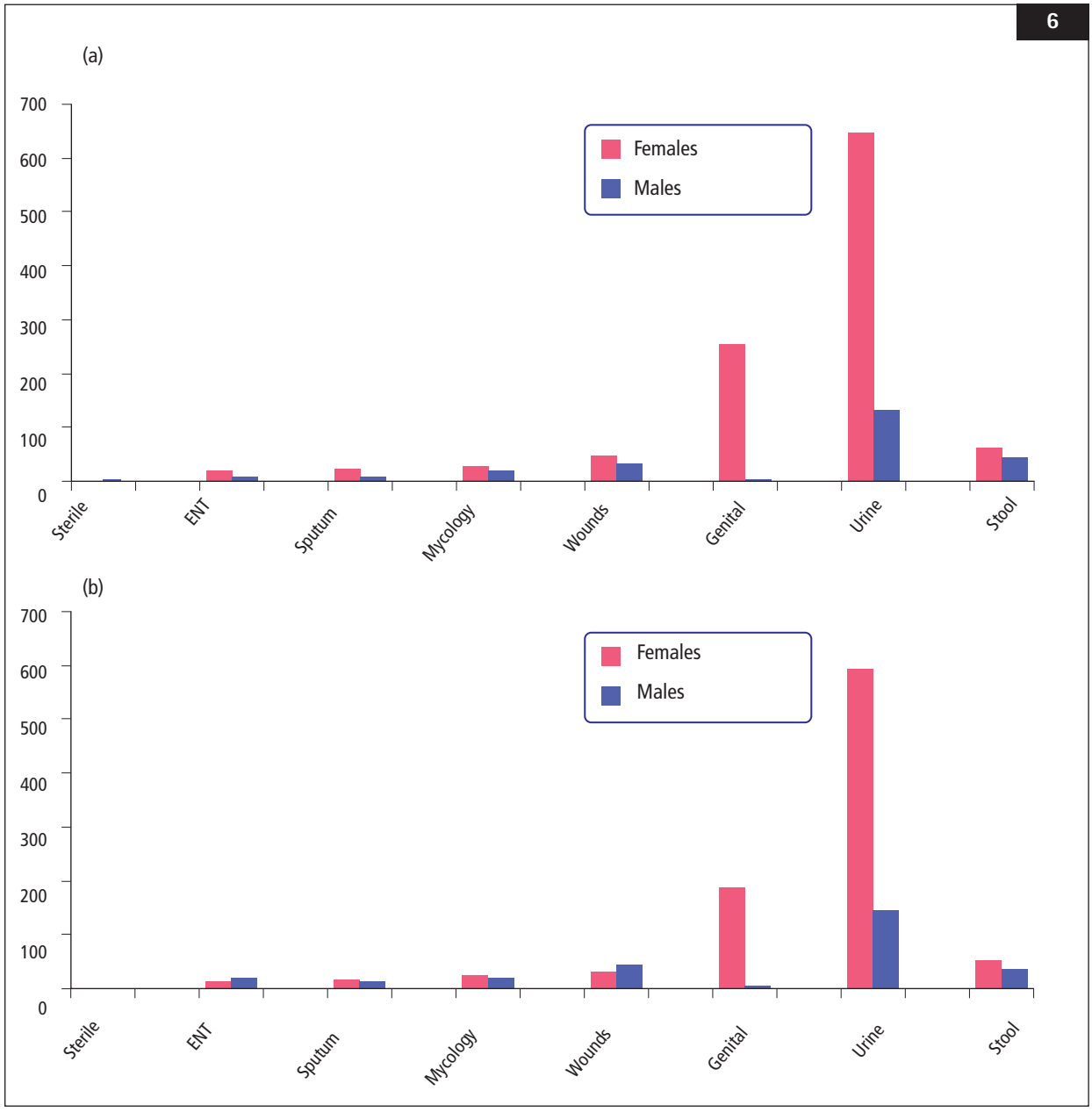


5 The critical steps outlined in **1** show the key stages in logistics/transport and the laboratory which can have an important impact on patient management. The example here compares the turnaround time for a mid-stream urine specimen taken in the morning with one taken late afternoon, adding an additional day to the turnaround time.

2009) to a medical microbiology laboratory serving a city in the UK with a population of 250 000 is shown in **6**. There were a total of 1338 specimens received in 1 week in October 2008 and 1230 in 1 week in April 2009. Urines accounted for 60% of the total, while genital site specimens accounted for about 20%. Overall, female patients contributed about 80% of all specimens, and accounted for 80% and 98% of specimens from the urinary tract and genital sites, respectively.

PUBLIC HEALTH AND THE COMMUNITY

Besides the interaction between the patient, the primary care physician, and the microbiology laboratory, the appropriate involvement of public health officers is essential, as infectious diseases know no boundaries. There are specific bodies responsible for managing public health, who must be involved promptly when the situation arises. For example, the primary care physician and nurse are in the ideal situation to recognize that a single case

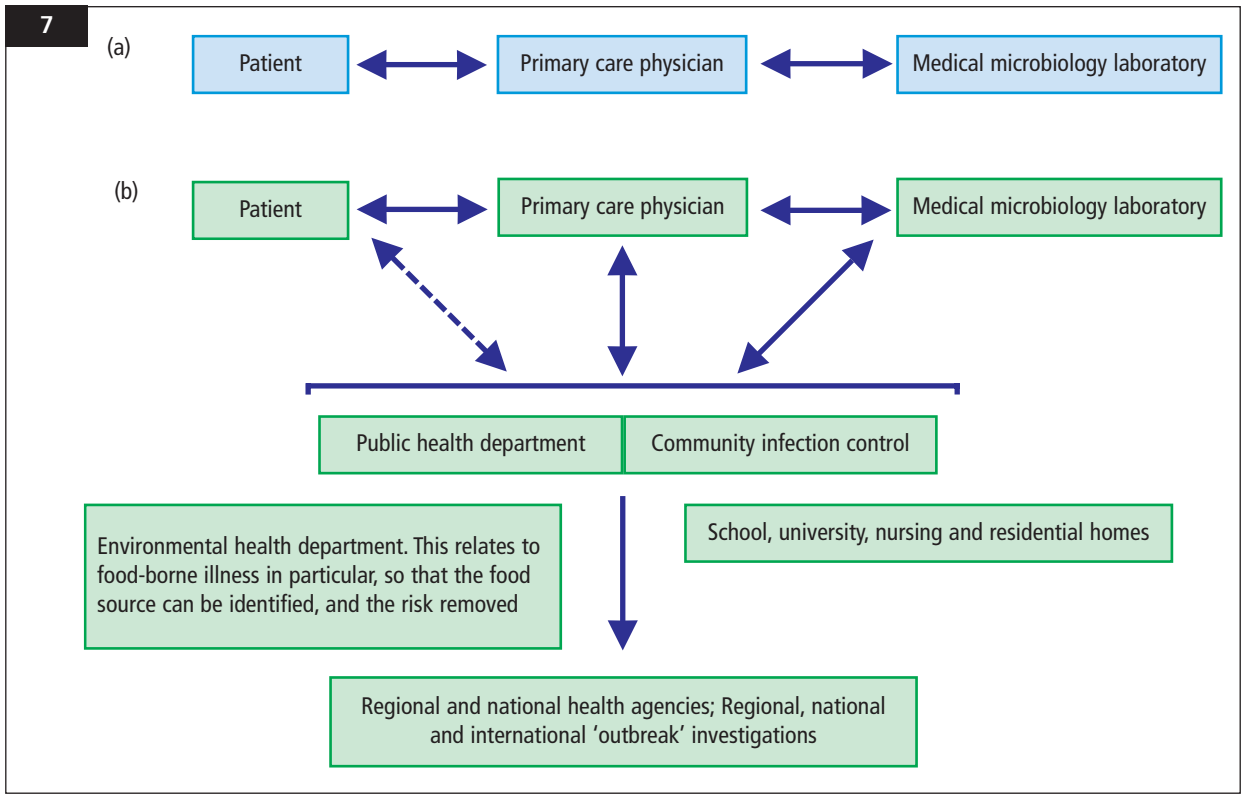


6 Analysis of the total number of bacteriology specimens received during a week in October 2008 (a) and April 2009 (b). Specimens are grouped according to laboratory 'benches': sterile sites (for example an aspirate of a bursa), ENT, sputum, mycology (dermatophytes), wound swabs, genital site swabs, urine specimens, and faecal specimens.

of diarrhoea may be the alert for an outbreak of 'food poisoning'. If the patient states that she/he was at a function where food and drink were served, and that others have the same illness, this information must be passed on to the relevant public health authority so that an investigation of a potential food-borne outbreak can be initiated immediately. Primary care physicians can have responsibility for nursing homes and residential care homes. When outbreaks of diarrhoea and vomiting occur, the primary care physician must inform the public health authority immediately. The interaction of all the officers involved in public health management is shown in 7. Officers of the local public health department are available 24/7 via the switchboard of the local acute hospital. In cases of food-borne illness and gastroenteritis, the local environmental health department (EHD) is an essential part of the system to protect public health, with the staff investigating all the circumstances of a food-poisoning incident in order to identify the source of the organism. In the USA, surveillance, data gathering, and investigations are coordinated by the Department of Health at state level.

Public health services have different structures, depending on the country. In England, the local health protection units (HPU) of the Health Protection Agency (HPA) are the link for primary care.[5] The HPU are staffed by consultants in communicable disease control, and they or their supporting staff should be informed promptly of any notifiable disease or condition.

National reference laboratories are an essential part of the public health service. In England, this is the Centre for Infections, Health Protection Agency, Colindale, London and in the USA this is the Center for Disease Control and Prevention, Atlanta, Georgia.[6] As an example of the role of reference


7
(a)
Patient
Primary care physician
Medical microbiology laboratory
(b)
Patient
Primary care physician
Medical microbiology laboratory
Public health department
Community infection control
Environmental health department. This relates to food-borne illness in particular, so that the food source can be identified, and the risk removed
School, university, nursing and residential homes
Regional and national health agencies; Regional, national and international 'outbreak' investigations

7 Public health in primary care. **(a)** The interaction between the patient, primary care physician and laboratory is more wide ranging than these three groups. **(b)** In addition to the patient, primary care physician and laboratory, many other factors influence health care. Public health activities, conducted in England through local health protection units of the Health Protection Agency, ensure that the wider community is also protected.

laboratories, medical microbiology departments in England submit isolates of salmonella and *Escherichia coli* O157 to the Enteric Pathogens Laboratory for 'typing' of strains within the species. This is particularly useful when an unusual strain of salmonella is identified from various geographical areas nationally and this is then an alert for a national investigation into the source (see *Salmonella* Stpaul below). For the purpose of this book, the terms public health department/doctor are used.

NOTIFICATION OF INFECTIOUS DISEASES AND CAUSATIVE AGENTS

In the UK, the Health Protection (Notification) Regulations of 2010 have brought up to date the notifiable diseases and causative agents that the local HPU need to be informed of as soon as possible.[7] Primary care physicians are responsible for notifying the conditions under Schedule 1 (Notifiable Diseases), while laboratories are responsible for notifying specific organisms under Schedule 2 (Causative Agents) (8). In the USA, the

8

Notification Regulations Schedule 1 Notifiable Diseases	Notification Regulations Schedule 2 Causative Agents	
Acute encephalitis	*Bacillus anthracis*	Lassa virus
Acute meningitis	*Bacillus cereus* (only if associated with *food poisoning)*	*Legionella* spp.
Acute infectious hepatitis	*Bordetella pertussis*	*Leptospira interrogans*
Acute poliomyelitis	*Borrelia* spp.	*Listeria monocytogenes*
Anthrax	*Brucella* spp.	Machupo virus (Bolivia haemorrhagic fever virus)
Botulism	*Burkholderia mallei*	Marburg virus
Brucellosis	*Burkholderia pseudomallei*	Measles virus
Cholera	*Campylobacter* spp.	Mumps virus
Diphtheria	Chikungunya virus	*Mycobacterium tuberculosis* complex
Enteric fever (typhoid or paratyphoid fever)	*Chlamydophila psittaci*	*Neisseria meningitidis*
Food poisoning	*Clostridium botulinum*	Omsk haemorrhagic fever virus
Haemolytic uraemic syndrome (HUS)	*Clostridium perfringens* (only if associated with food poisoning)	*Plasmodium falciparum, P. vivaz, P. ovale, P. malariae, P. knowlesi**
Infectious bloody diarrhoea	*Clostridium tetani*	Polio virus wild or vaccine types
Invasive group A streptococcal disease and scarlet fever	*Corynebacterium diphtheriae*	Rabies virus (classical rabies and rabies-related lyssaviruses)
Legionnaires' disease	*Corynebacterium ulcerans*	*Rickettsia* spp.
Leprosy	*Coxiella burnetii*	Rift valley fever virus
Malaria	Crimean–Congo haemorrhagic fever virus	Rubella virus
Measles	*Cryptosporidium* spp.	Sabia virus (a South American haemorrhagic fever virus)
Meningococcal septicaemia	Dengue virus	*Salmonella* spp. (including *S. typhi* and *S. paratyphi*)
Mumps	Ebola virus	SARS coronavirus
Plague	*Entamoeba histolytica*	*Shigella* spp.
Rabies	*Francisella tularensis*	*Streptococcus pneumoniae* (invasive)
Rubella	*Giardia lamblia*	*Streptococcus pyogenes* (invasive)
SARS	Guanarito virus (Venezuela haemorrhagic fever virus)	Varicella zoster virus
Smallpox	*Haemophilus influenzae* (invasive)	Variola virus
Tetanus	Hanta virus	Verocytotoxigenic *Escherichia coli* (including *Escherichia coli* O157)
Tuberculosis	Hepatitis A, B, C, Delta, and E viruses (all acute and chronic cases, as relevant)	*Vibrio cholerae*
Typhus	Influenza virus	West Nile virus
Viral haemorrhagic fever (VHF)	Junin virus (Argentina haemorrhagic fever virus)	Yellow fever virus
Whooping cough	Kyasanur forest disease virus	*Yersinia pestis*
Yellow fever		

8 The list of notifiable diseases (for which the attending clinician is responsible) and causative agents (for which the laboratory is responsible for) listed in the Health Regulations (Notifications) Act of 2010 for England and Wales.[7] These are to be conveyed to the local HPU at the earliest opportunity.

Note *Plasmodium* spp. are usually screened for in blood films in haematology laboratories in the UK.

list of notifiable diseases is more comprehensive and is updated annually (**9**).[8] In the USA, the organization coordinating the various branches of public health is the Center for Disease Control and Prevention, Atlanta, Georgia. There is some variation in notification at state level.

Gastroenteritis is a good example of the effect that infections have in the community. Outbreaks may be restricted to one family, but not infrequently they affect the wider community, and food-poisoning incidents are regularly reported from social functions, such as wedding receptions. Reporting notifiable conditions promptly is essential to detect an outbreak at the earliest opportunity. The information submitted is collated locally, regionally, or on occasion nationally. This enables the likely source of an organism to be identified, so the hazard risk can be identified and removed.

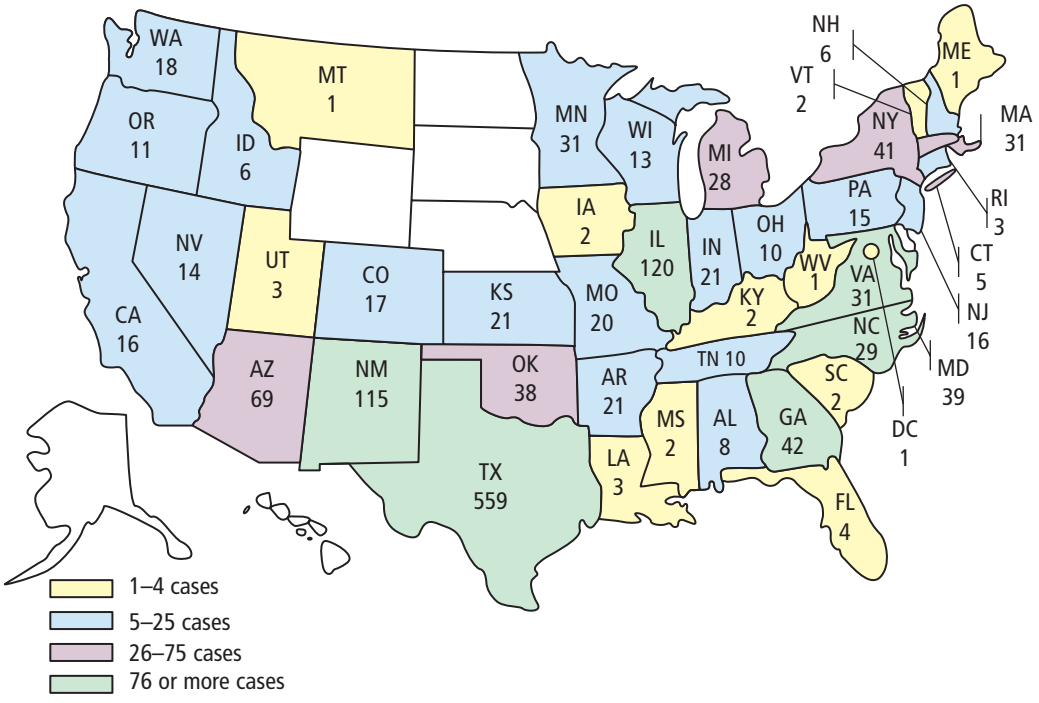
There are many interesting examples. An outbreak of *Salmonella* Stpaul in the USA in 2008 showed that over 1400 individuals from 43 states were infected with the same organism that was subsequently identified in jalapeno peppers imported from Mexico (**10, 11**).[9] Outbreaks of food-borne infection may be on a massive scale; in

9

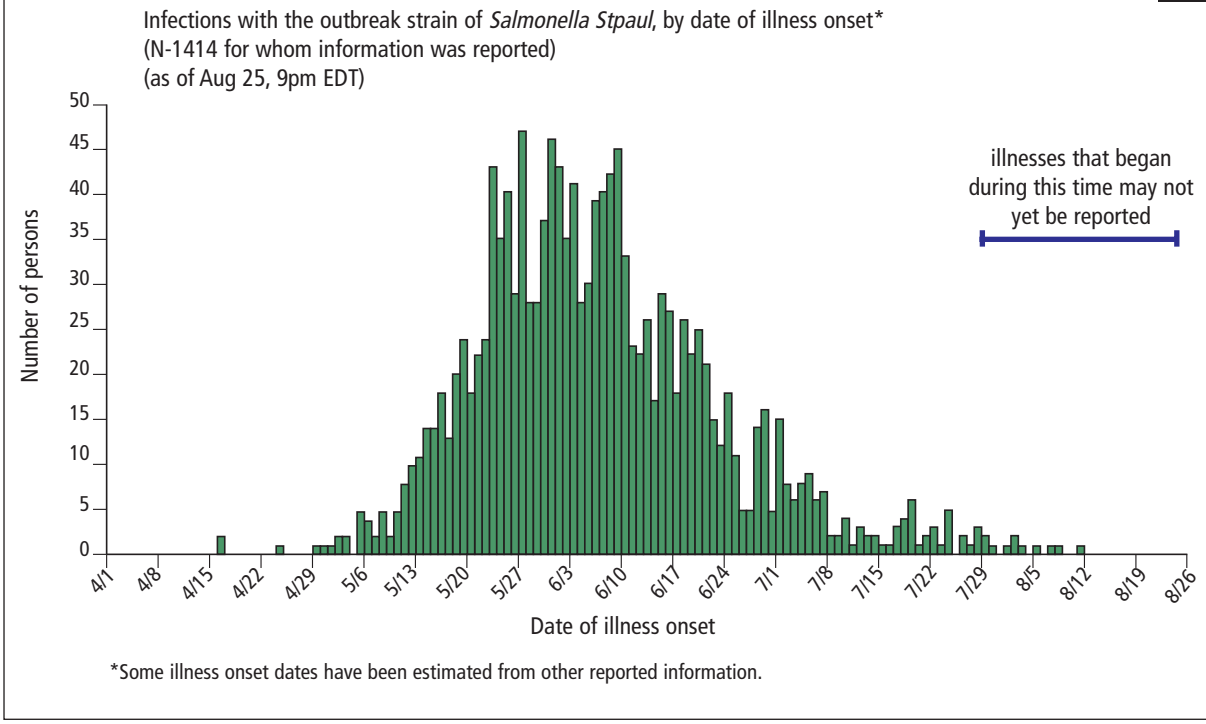
- Anthrax
- Arboviral neuroinvasive and non-neuroinvasive diseases
  - California serogroup virus disease
  - Eastern equine encephalitis virus disease
  - Powassan virus disease
  - St Louis encephalitis virus disease
  - West Nile virus disease
  - Western equine encephalitis virus disease
- Botulism
  - Food-borne
  - Infant
  - Other (wound and unspecified)
- Brucellosis
- Chancroid
- *Chlamydia trachomatis* infection
- Cholera
- Cryptosporidiosis
- Cyclosporiasis
- Dengue
  - Dengue fever
  - Dengue haemorrhagic fever
  - Dengue shock syndrome
- Diphtheria
- Ehrlichiosis/anaplasmosis
  - *Ehrlichia chaffeensis*
  - *Ehrlichia ewingii*
  - *Anaplasma phagocytophilum*
  - Undetermined
- Giardiasis
- Gonorrhoea
- *Haemophilus influenzae*, invasive disease
- Hansen disease (leprosy)
- Hantavirus pulmonary syndrome
- Haemolytic uraemic syndrome, post-diarrhoeal
- Hepatitis
  - Hepatitis A, acute
  - Hepatitis B, acute
  - Hepatitis B, chronic
  - Hepatitis B virus, perinatal infection
  - Hepatitis C virus, acute
  - Hepatitis C, chronic
- HIV infection
  - HIV infection, adult/adolescent (age ≥13 years)
  - HIV infection, child (age ≥18 months and <13 years)
  - HIV infection, paediatric (age <18 months)
- Influenza-associated paediatric mortality
- Legionellosis
- Listeriosis
- Lyme disease
- Malaria
- Measles
- Meningococcal disease
- Mumps
- Novel influenza A virus infections
- Pertussis
- Plague
- Poliomyelitis, paralytic
- Poliovirus infection, nonparalytic
- Psittacosis
- Q Fever
  - Acute
  - Chronic
- Rabies
  - Rabies, animal
  - Rabies, human
- Rubella
- Rubella congenital syndrome
- Salmonellosis
- Severe acute respiratory syndrome–associated coronavirus (SARS-CoV) disease
- Shiga toxin-producing *Escherichia coli* (STEC)
- Shigellosis
- Smallpox
- Spotted fever rickettsiosis
- Streptococcal toxic-shock syndrome
- *Streptococcus pneumoniae*, invasive disease
- Syphilis
  - Primary
  - Secondary
  - Latent
  - Early latent
  - Late latent
  - Latent, unknown duration
  - Neurosyphilis
  - Late, non-neurological
  - Stillbirth
  - Congenital
- Tetanus
- Toxic-shock syndrome (other than streptococcal)
- Trichinellosis (trichinosis)
- Tuberculosis
- Tularaemia
- Typhoid fever
- Vancomycin-intermediate *Staphylococcus aureus* (VISA)
- Vancomycin-resistant *Staphylococcus aureus* (VRSA)
- Varicella (morbidity)
- Varicella (deaths only)
- Vibriosis
- Viral haemorrhagic fevers
  - Arenavirus
  - Crimean– Congo haemorrhagic fever
  - Ebola virus
  - Lassa virus
  - Marburg virus
- Yellow fever

9 The list of the Nationally Notifiable Infections conditions in the USA 2010, updated on the CDC webpage.[8] See www.cdc.gov/ncphi/disss/nndss/phs/infdis2010.htm

10



11



10, 11 Information on the CDC webpage showing details of an outbreak of *Salmonella* Stpaul in the USA in 2008.[9] **(10)** The number of cases/state who were infected after consuming food prepared with contaminated jalapeno peppers. **(11)** The epidemiological 'outbreak curve' associated with this outbreak. (Adapted, with permission from the CDC, Atlanta, USA.)

the USA in 1995, over 250 000 individuals were estimated to have been affected by a national outbreak of salmonella food poisoning. Here a single batch of ice cream had been inadvertently mixed during preparation with unpasteurized fresh egg slurry contaminated with the salmonella strain.[10]

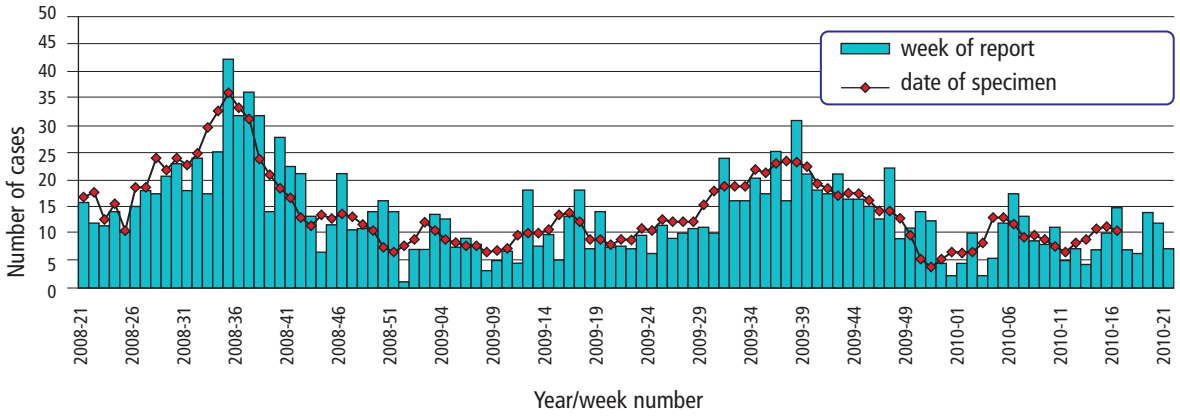
It is often difficult to obtain the precise size of an outbreak. There is likely to be a wide spectrum of illness from asymptomatic through to severely ill, and of those with mild symptoms, many may not seek medical help. Of those who do, only a proportion submits a specimen for examination, and the organism in turn is only identified in some of these specimens. As an extreme example, for every case of norovirus reported, usually an unpleasant short-lived and self-limiting illness, it is estimated that over 1500 cases go unreported.[11] This must equate to several millions being affected in a period of several weeks when norovirus is active nationally. The consequences in terms of work- and school-days lost are considerable. In the case of salmonella and campylobacter, the ratio of reported to actual cases is not as dramatic, being about 1:4 and 1:8, respectively.[11] The large difference in the ratios between norovirus and salmonella/campylobacter can be attributed in part to the ease of transmission (person to person) of norovirus and that most people do not seek medical advice as the associated illness is generally mild and of a short-lived nature.

Laboratories in England update their regional HPA epidemiological unit electronically on a weekly basis with details of the number of specific pathogens that have been identified in the laboratory. This information is collated, and the combined data are used to produce graphical information. An example of the annual activity of key organisms in an area of the UK, based on the submissions of 15 medical microbiology laboratories is shown in **12–20**. Information in the USA is available on the Centres for Disease Control (and Prevention) (CDC) webpage, and examples include the annual geographical distribution of organisms; examples showing cryptosporidium and Lyme disease are shown in **21, 22**, page 24.[12, 13] The usefulness of the examples given in **12–20** is clear, as an awareness and understanding of current activity of key organisms in the community can be of use when managing individual patients.

12–20 The activity of a number of key organisms in an area of the UK is obtained by collating the data submitted by 15 medical microbiology laboratories. **12–19**: Faecal specimens; **20**: Respiratory specimens. The information shows that there is a significant burden of campylobacter throughout the year, whereas rotavirus, influenza, and RSV have distinct periods of activity annually. The relative number of individual cases (y axis) for campylobacter and *Escherichia coli* O157 can be compared. (Adapted from data made available by the HPA West Midlands Regional Epidemiology Unit, with permission.)

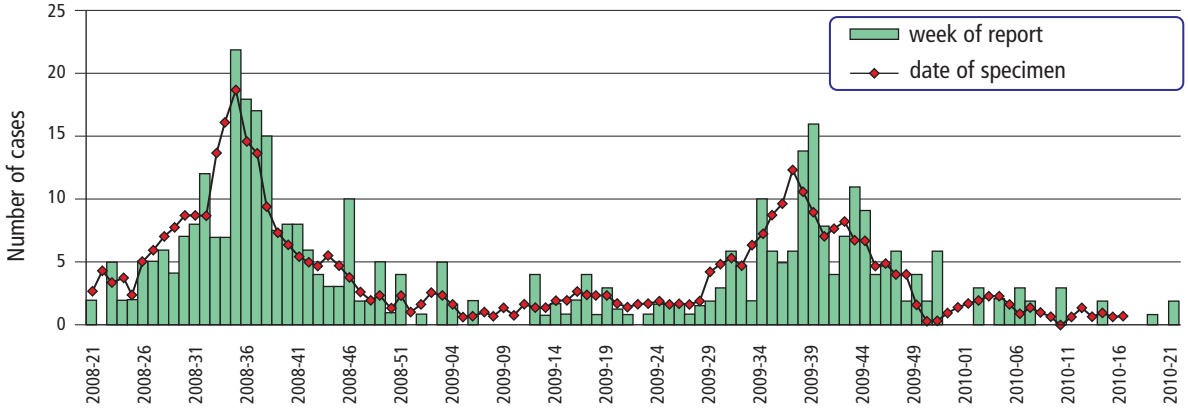
12

LABORATORY DATA: All *Salmonella*, by week of report to RE (CoSurv) and 3-weekly average by date of specimen (Lab-base)



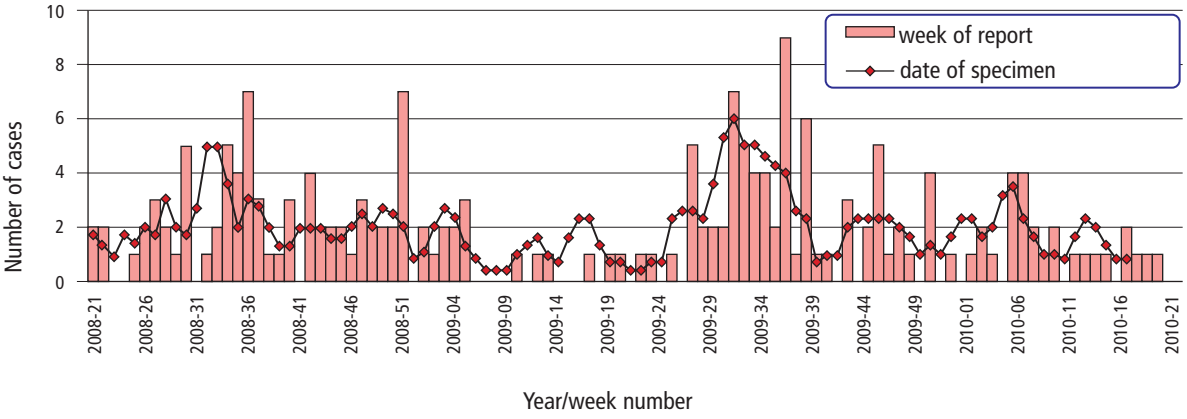
13

LABORATORY DATA: *Salmonella enteritidis*, by week of report to RE (CoSurv) and 3-weekly average by date of specimen (Lab-base)



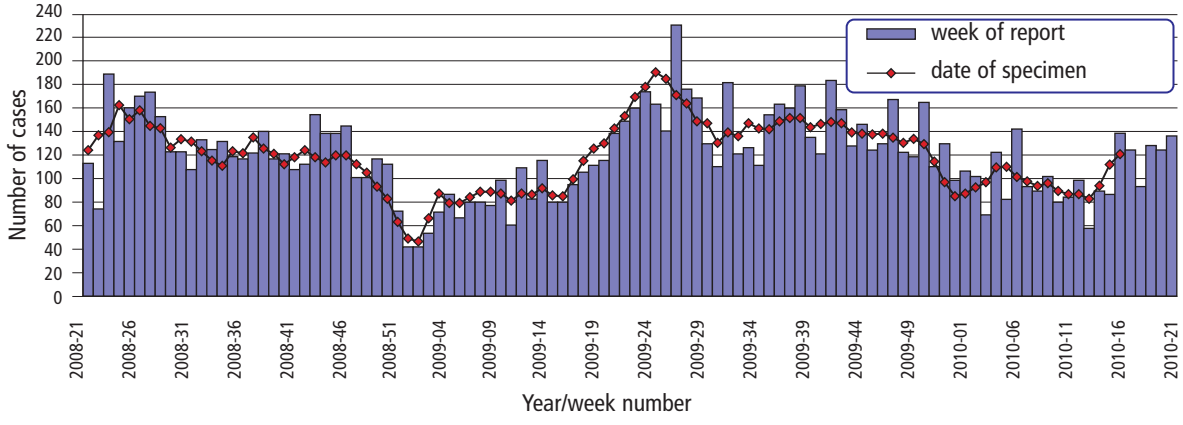
14

LABORATORY DATA: *Salmonella typhimurium*, by week of report to RE (CoSurv) and 3-weekly average by date of specimen (Lab-base)

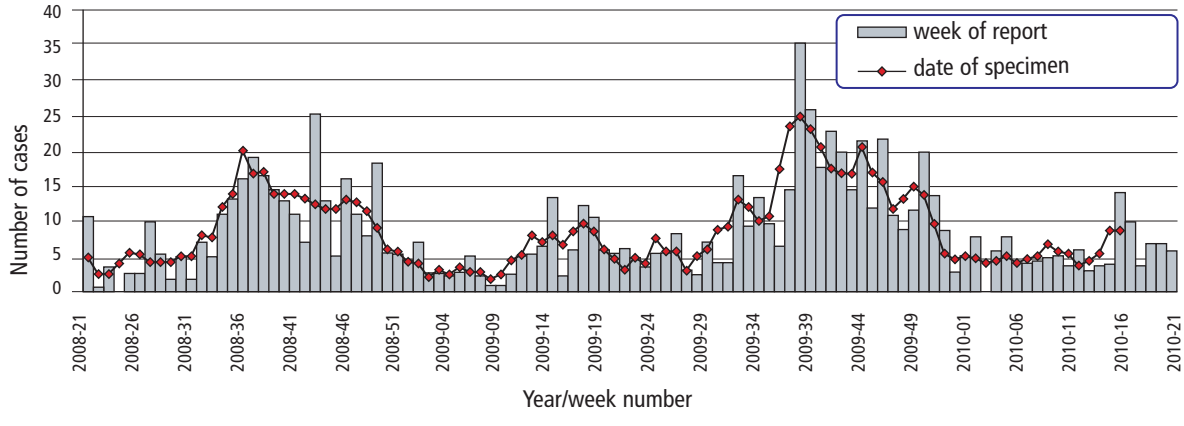


(*Continued*)

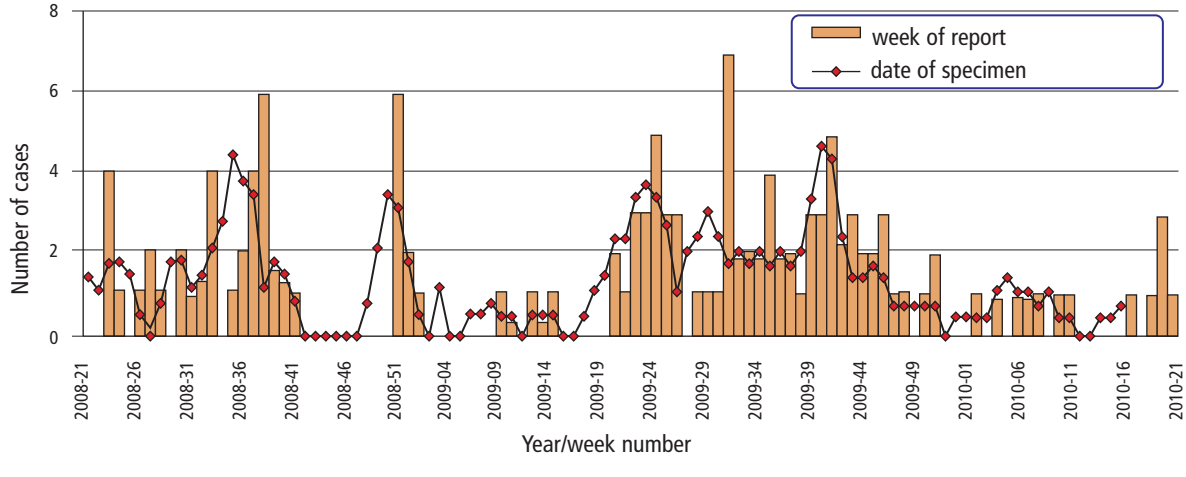
15 LABORATORY DATA: All *Campylobacter*, by week of report to RE (CoSurv) and 3-weekly average by date of specimen (Lab-base)



16 LABORATORY DATA: *Cryptosporidium*, by week of report to RE (CoSurv) and 3-weekly average by date of specimen (Lab-base)

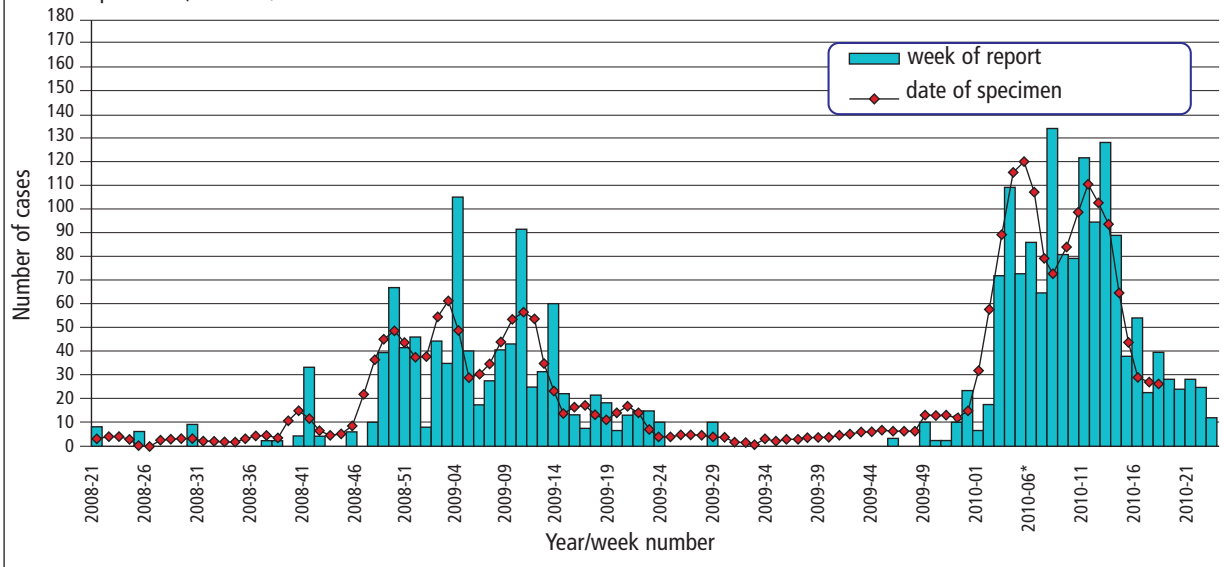


17 LABORATORY DATA: *E. Coli* O157, by week of report to RE (CoSurv) and 3-weekly average by date of specimen (Lab-base)



18

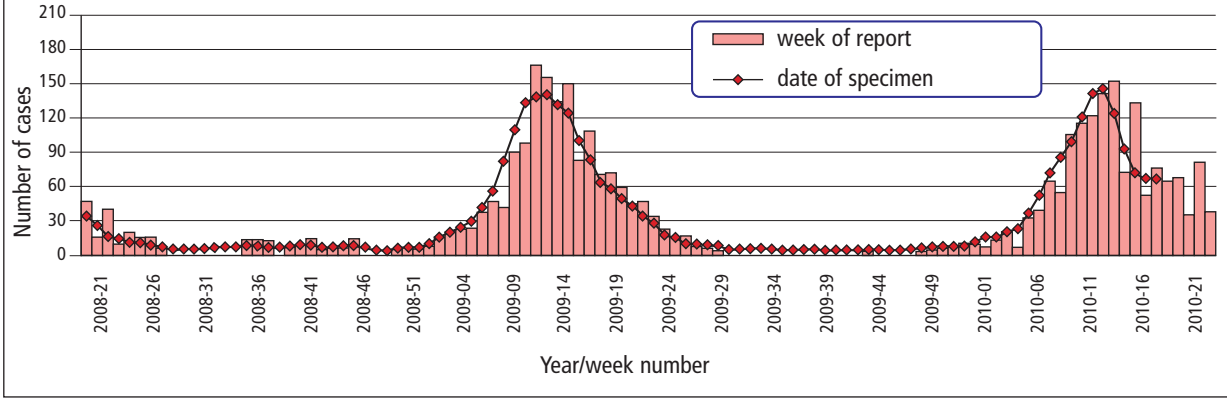
LABORATORY DATA: *Norovirus (SRSV)*, by week of report to RE (CoSurv) and 3-weekly average by date of specimen (Lab-base)



*Please note batch reporting has contributed to high numbers of norovirus reports in week 6 of 2010.

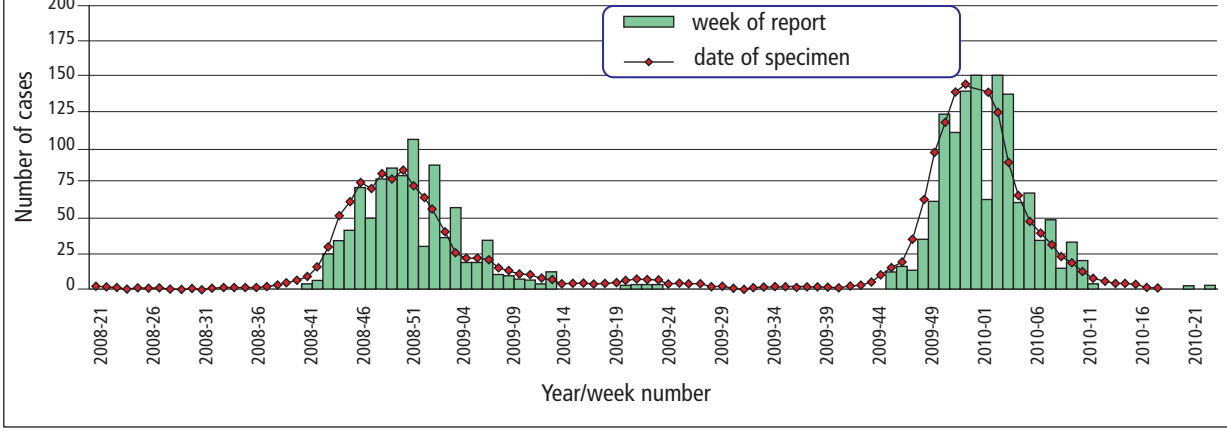
19

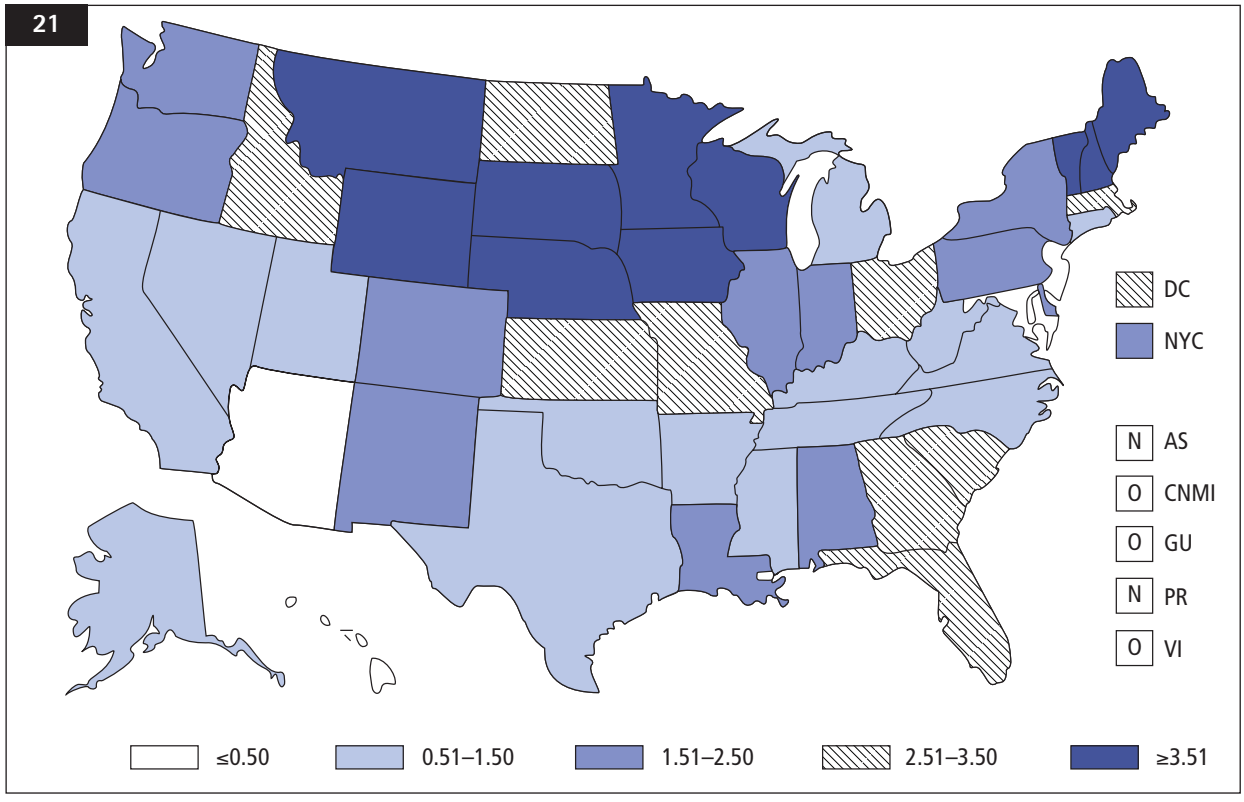
LABORATORY DATA: *Rotavirus*, by week of report to RE (CoSurv) and 3-weekly average by date of specimen (Lab-base)

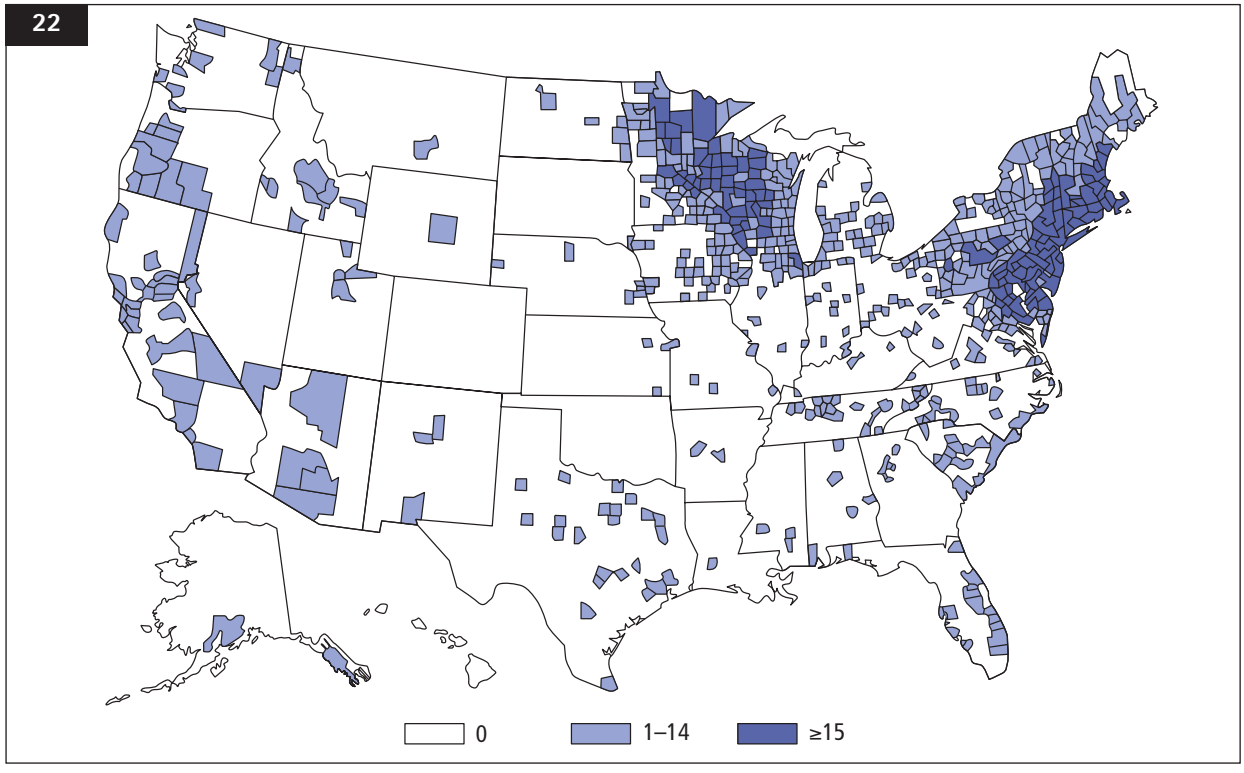


20

LABORATORY DATA: *RSV*, by week of report to RE (CoSurv) and 3-weekly average by date of specimen (Lab-base)







21, 22 Incidence of (**21**) cryptosporidiosis in 2005 (by jurisdiction), and (**22**) Lyme disease, average rate 1992–2006 (reported by county of residence) as cases/100 000 population in the USA. (Adapted, with permission from the CDC, Atlanta, USA.)

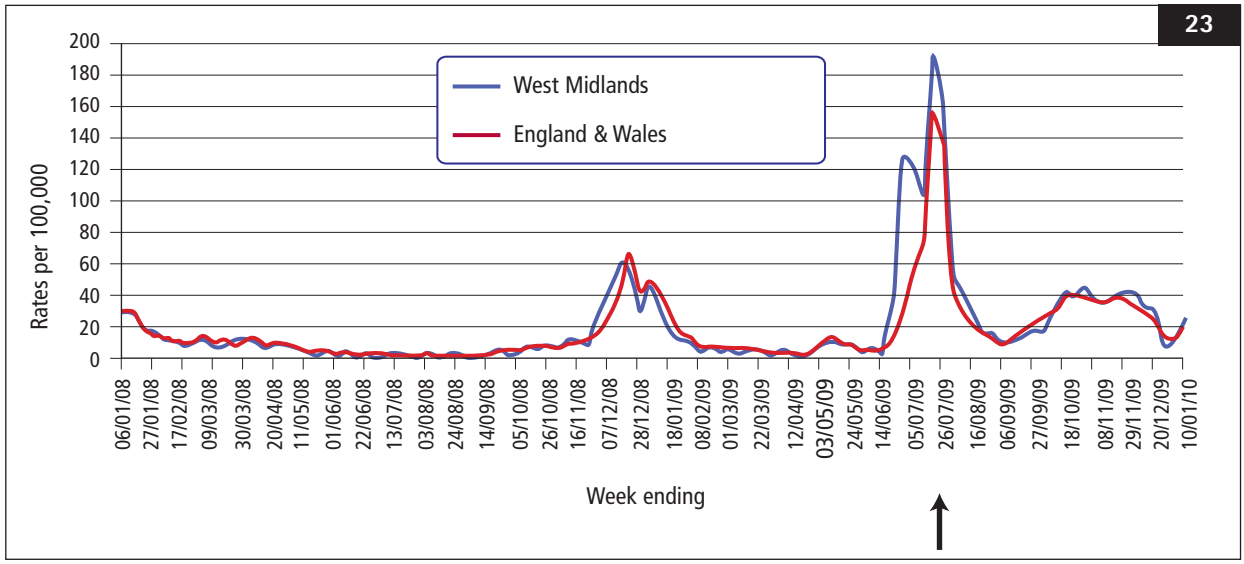
The epidemiology of 'new' infections is exemplified by the swine flu pandemic in 2009, and the stress that this put on health care in many parts of the world. Figure **23** shows the 'epidemiological curve' of swine flu in an area of the UK, while **24–26** (overleaf) summarizes the CDC data for the USA, highlighting the total number of cases, hospital admissions, and deaths.[14] Primary care is in the 'front-line' in these situations, and the key links identified in **7** must be in place to manage these complex situations.

SUMMARY AND KEY POINTS

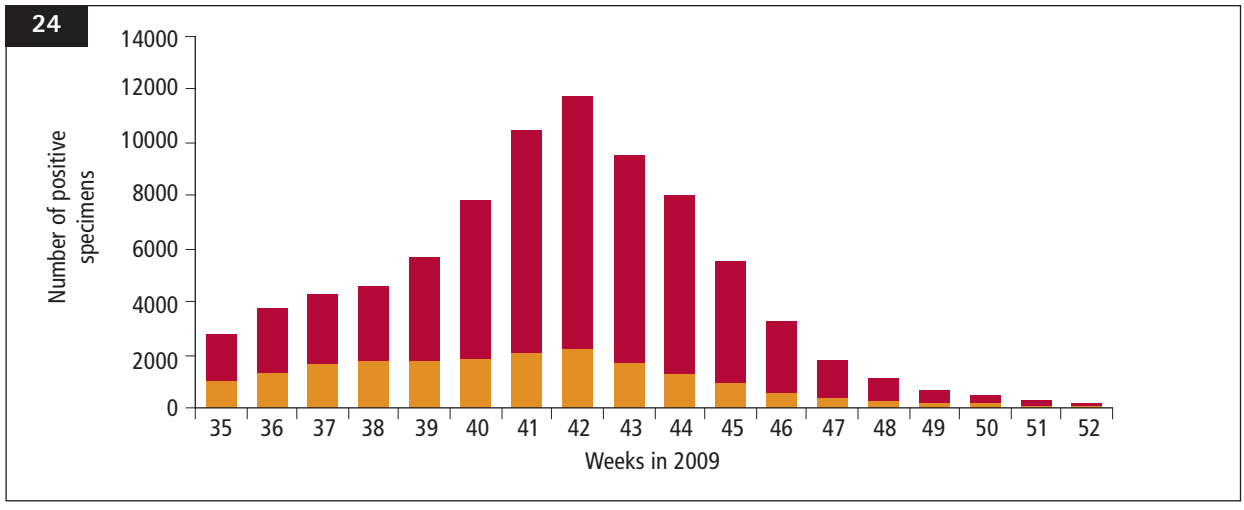
This chapter introduces some key issues with the management of infection in the community. On a day-to-day basis, the most striking information is that presented in **6**, which shows that the majority of specimens taken in the community setting are urines and genital swabs, mainly from female patients. There must be many opportunities to improve all the critical steps outlined in **1** for every specimen type. It should be possible for primary care practices/clinics to start by targeting the urine specimen, and to set up ongoing training on the basis of the critical steps. The local medical microbiology department should be involved. The end result must be more efficient and safer patient management, which at the same time will save resources and money.

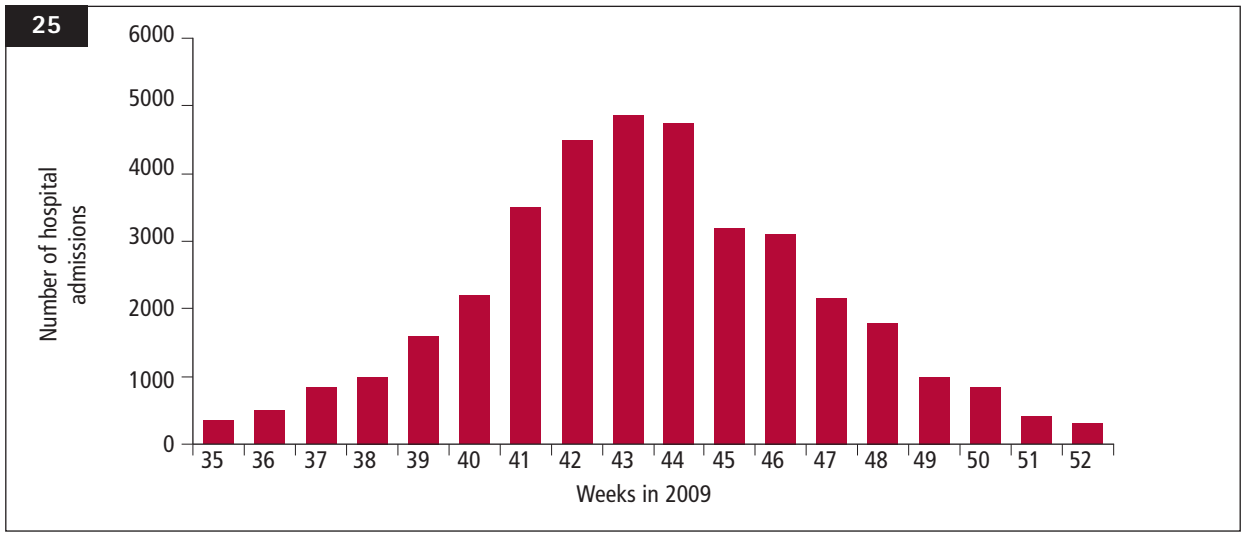
In summary the following points should be noted:

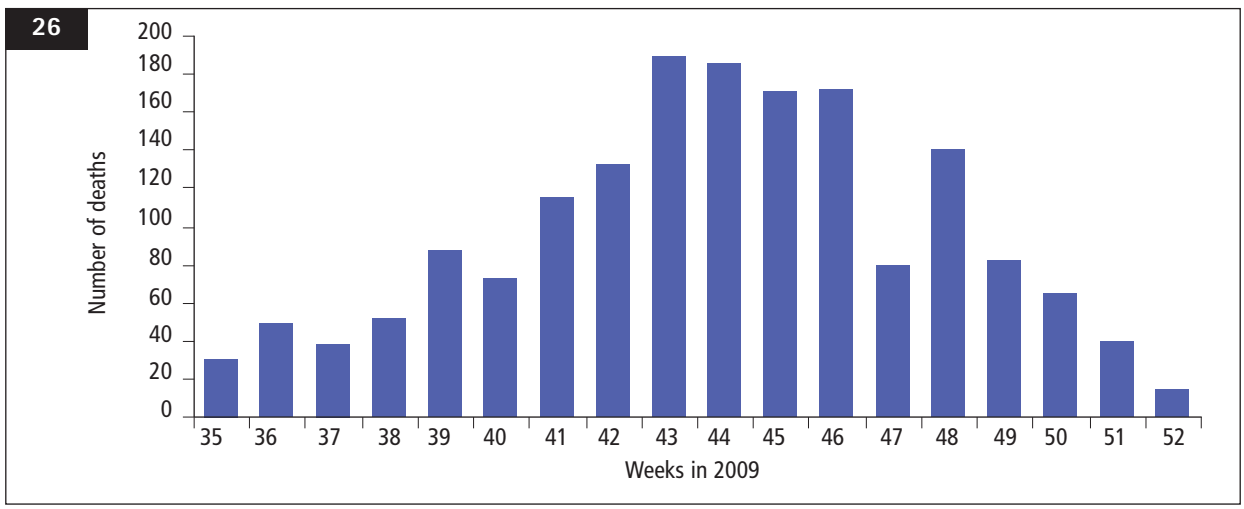
- This book is unique in that it is NOT a standard microbiology text. Instead, it focuses on key areas outside of the laboratory that have such an important role in managing the patient.
- Every day, numerous specimens are submitted to the laboratory where either there was no clinical indication to send one in the first instance, or it was poorly collected. A mixed growth of organisms or growth of an organism other than the pathogen, or both is then reported. This leads to antibiotics being given inappropriately or treatment of the wrong organism.
- In chapters 3–10, the pathway from deciding to take a specimen through to interpretation of the report and considering treatment follows the seven critical steps outlined in this chapter, which are both in and outside of the laboratory.
- By concentrating on the steps highlighted in each chapter through regular training sessions in the practice/clinic, patient care will improve and real savings made.



23 Epidemiological curve showing consultations for influenza-like illness in primary care in the West Midlands area, and overall in England and Wales as cases/100 000 population. The dramatic nature of the swine flu situation in mid-year is clearly shown (arrow). (Adapted from data made available by the HPA West Midlands Regional Epidemiology Unit and the Royal College of General Practitioners Research and Surveillance Centre, with permission.)







24–26 A summary of the swine flu situation in the USA between weeks 35 and 52 in 2009; influenza-positive tests reported to CDC by USA WHO/NREVSS collaborating laboratories. (Adapted with the permission of the CDC, Atlanta, USA). (**24**) Influenza A (2009) H1N1: red bars; influenza A subtyping not performed: yellow bars. (Other subtypes and influenza B are not included in this adaptation; their numbers here are too small to observe here.) (**25**) Number of hospital admissions. (**26**) Number of deaths.

2

Organisms and Antibiotics

- Introduction
- A practical problem
- Common organisms associated with infection in the community
- The activity of antibiotics against bacteria
- Antibiotic guidelines to use in common infections
- Intravenous antibiotic use in the community; outpatient parenteral antibiotic therapy (OPAT)
- The role that antibiotics have in predisposing to *Clostridium difficile* infection, the agent responsible for CDAD
- The expectations of patients and parents
- Summary and key points

INTRODUCTION

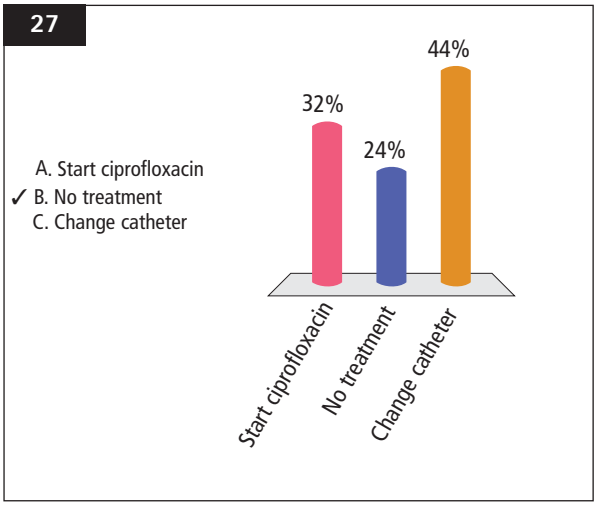
This chapter summarizes some features of more common organisms that are reported by the laboratory in swabs (eye, ENT, high vaginal swab [HVS], and wound), sputum, and urine specimens, in relation to their usual clinical relevance in primary care. Information is given on aspects of bacterial structure, antibiotic resistance mechanisms, and the range of activity of antibiotics against the bacteria discussed. This is to provide background information for each 'specimen type' chapter that follows. A short summary of outpatient parenteral antibiotic therapy (OPAT) is included. The relationship of antibiotic use in the hospital and community to *Clostridium difficile*-associated diarrhoea (CDAD) is emphasized.

A PRACTICAL PROBLEM

Consider this scenario that was presented to a group of 130 primary care physicians: a laboratory report on a urine specimen collected from a 76-year-old male, a nursing home resident, who has a long-term catheter in place, shows a profuse growth of *Pseudomonas aeruginosa*, sensitive to ciprofloxacin. The clinical details state: 'Offensive smelling urine'. The various options to consider and the summary of the responses of the primary care physician are shown in **27**.

This scenario is not uncommon. When analysed using the critical steps outlined in **1**, page 11 of importance is that critical steps 1 and 7 have been breached. A urine specimen should only have been collected if the patient was symptomatic. Offensive smelling urine is not an indication in its own right, as bacteriuria is an inevitable consequence of long-term catheterization. Urine culture was positive, in this instance growing pseudomonas, which is not an unexpected finding. Of the 130 primary care physicians, 44% would have changed the catheter, and 32% would have prescribed ciprofloxacin. Over 30% of the respondents breached critical step 7 by administering an antibiotic based on the laboratory report, when there was no clinical need to do so. Before initiating any treatment, critical step 1 should have been reviewed. The inappropriate use of any antibiotic incurs the risk of side-effects. Ciprofloxacin could select resistant bacteria, either a quinolone-resistant variant of the pseudomonas (meaning that no oral therapy would be available to treat an infection with this organism should it arise in the future), or for other resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) and the extended-spectrum β-lactamase-producing (ESBL) 'coliforms'. There is clear evidence that the more widespread and uncontrolled antibiotic use is, the more likely that resistant bacteria will be selected.[1–3] Most importantly, the unnecessary use of the antibiotic also places the patient at risk of CDAD.[4–8] This is not only a hospital problem, but occurs in the community as well.[9] This scenario highlights how the simple act of submitting a specimen can unnecessarily set up a chain of events that is not only wasteful of resources, but may result in inappropriate management with disastrous consequences.

27



27 This scenario was presented to a group of 130 primary care physicians, who were asked which of the three options they would choose. The correct answer is B; the responses, expressed as percentages are shown in the bar chart.

COMMON ORGANISMS ASSOCIATED WITH INFECTION IN THE COMMUNITY

A list of common organisms to consider in primary care is shown in **28**, highlighting their relevance when identified in a particular clinical condition and specimen type. Bacteria are grouped into gram-positive and gram-negative, and the details of the cell wall structure accounting for this grouping are shown in **29**, page 34.

28

Gram-positive bacteria

Staphylococcus aureus (methicillin-sensitive; MSSA)
Staphylococcus aureus (methicillin-resistant; MRSA)
Coagulase-negative staphylococcus (CNS)

Both MSSA and MRSA have cell wall components that can bind to, and coagulate fibrin, causing plasma to clot, and are thus 'coagulase-positive'. The correlation between coagulase production and pathogenicity of *Staphylococcus aureus* provides a simple virulence marker and laboratory test to differentiate the pathogenic *Staphylococcus aureus* from the relatively nonpathogenic CNS. CNS such as *Staphylococcus saprophyticus* can cause UTI in otherwise healthy young women. They can also cause infections in prostheses, such as joint replacements. Generally in the community setting, they should be regarded as colonizing skin flora

Enterococci
Group A streptococcus (GAS)
Group B streptococcus (GBS)
Group C streptococcus (GCS)
Group G streptococcus (GGS)
Streptococcus pneumoniae

Gram-negative bacteria

Haemophilus influenzae
Escherichia coli (including ESBL-producers), a 'coliform'
Klebsiella pneumoniae (including ESBL-producers), a 'coliform'
Proteus, a 'coliform'
Pseudomonas aeruginosa

'Coliforms' is a collective term, frowned upon by some, that includes those gram-negative bacteria that can grow both aerobically and anaerobically (facultative), that usually ferment glucose and grow on selective (bile-salt containing) media used for isolating enteric (bowel) bacteria. In addition to *Escherichia coli* and *Klebsiella* spp., salmonella, shigella, enterobacter, and serratia are also 'coliforms'

Anaerobes (gram-positive and gram-negative)

Clostridia
Anaerobic streptococci
Oral anaerobes; e.g. Prevotella
Bowel anaerobes; e.g. Bacteroides

(*Continued*)

28 A list of the common bacteria to consider in primary care that are reported by the laboratory in swabs (eye, ENT, HVS, and wound), sputum, and urine specimens, in relation to their usual clinical relevance in primary care. The majority of bacterial infections are caused by a relatively small number of organisms.

28

Gram-positive	Specimen	Comment
Staphylococcus aureus (MSSA, MRSA)	Eye swab	Can cause conjunctivitis Colonization can be present in the elderly
	ENT swab	Can cause otitis externa. Nose and throat carriage occur
	Sputum	Sputum samples can be contaminated with MSSA and MRSA from throat carriage. (Pneumonia can occur in the community, and can arise after influenza infection. PVL-producing isolates can cause life-threatening haemorrhagic pneumonia)*
	HVS	Not a recognized cause of a vaginal discharge. May be associated with infection of Bartholin's gland, vulval abscess, post-partum, or post-surgery. Toxic shock syndrome associated with tampon use can occur. Vaginal and perineal colonization occurs
	Urine	An uncommon cause of UTI
	Wound/ulcer swab	Associated with boils, furuncles, impetigo, and cellulitis. Colonization of chronic leg ulcers occurs, and antibiotics should not be given unless there is evidence of infection. Common cause of post-surgical wound infections. PVL* isolates can cause life-threatening skin and soft tissue infection
Coagulase-negative staphylococci (CNS)	Eye swab	Not a pathogen in conjunctivitis. It can cause endophthalmitis following cataract surgery
	ENT swab	Not a pathogen
	Sputum	Not a pathogen
	HVS	Not a pathogen
	Urine	*Staphylococcus saprophyticus* is recognized as a cause of uncomplicated UTI in young sexually-active women
	Wound/ulcer swab	Not usually a pathogen, but stitch-site abcesses can occur in post-surgical wounds
Enterococci	Eye swab	Not a recognized cause of conjunctivitis
	ENT swab	Not a recognized cause of ENT infections
	Sputum	Not a recognized cause of pneumonia
	HVS	Not a recognized cause of vaginal discharge. May be isolated, along with other bacteria from pus obtained from the pelvic abscess of a patient with chronic pelvic inflammatory disease (PID)
	Urine	A recognized cause of cystitis
	Wound/ulcer swab	Can colonize wounds and ulcers; an unlikely pathogen, but can be isolated from a polymicrobial abscess following abdominal surgery
Group A streptococcus (GAS)		This is a particularly unpleasant bacterium. When identified in a clinical specimen, the acronym 'A for Always' should be considered for treatment
	Eye swab	Can cause conjunctivitis. Unlikely to colonize; treatment should be considered
	ENT swab	Can cause otitis externa and otitis media. Common cause of bacterial pharyngitis. Asymptomatic nose and throat carriage can occur
	Sputum	GAS pneumonia is uncommon
	HVS	When found in association with a discharge, always treat. Can cause vulvitis, perianal cellulitis in pre-pubertal girls. GAS is an important cause of puerperal sepsis. Colonization not recognized.

* Certain isolates produce the Panton–Valentine leukocidin (PVL) toxin. This can be associated with recurrent boils, severe soft tissue infection, and pneumonia (see Chapter 5). Other toxin-based diseases include toxic shock syndrome (TSS) caused by TSS-toxin producing strains, and staphylococcal scalded skin syndrome (SSSS) caused by epidermolytic toxin- (ET) producing strains. Enterotoxin-producing strains growing in contaminated food can initiate vomiting and diarrhoea within 1–4 hours of food consumption; recovery is usually rapid.

28

	Urine	Very uncommon finding in the urinary tract, and its presence suggests a vaginal source, or in the male, balanitis
	Wound/ulcer swab	Can cause erysipelas, impetigo, cellulitis, perianal cellulitis, necrotizing fasciitis, and surgical wound infection. *Colonization of chronic ulcers is most unlikely*, and when GAS is reported, treatment should be given
	Specimen	**Comment**
Group B streptococcus (GBS)	Eye swab	Unlikely cause of conjunctivitis (excluding neonates)
	ENT swab	Unlikely cause of infection, including pharyngitis
	Sputum	GBS pneumonia is uncommon
	HVS	Not a recognized cause of a vaginal discharge. It can be associated with post-partum or post-surgery wound infections Colonization can occur in up to 40% of women. This is only relevant in neonatal infections in pre-term labour and prematurity, where neonatal sepsis and meningitis can occur. While antibiotic prophylaxis can be given to mothers at delivery to protect the child, there is no evidence to treat GBS carriage during pregnancy. See Chapter 10
	Urine	Recognized cause of UTI
	Wound/ulcer swab	An uncommon cause of cellulitis, but may cause soft-tissue infections in diabetics in particular. Colonization of chronic ulcers can occur. Resistant to flucloxacillin/dicloxacillin and tetracyclines
Group C streptococcus (GCS)	Eye swab	Can cause conjunctivitis
Group G streptococcus (GGS)		Unlikely to colonize; treatment should be considered
	ENT swab	Can cause otitis externa and otitis media. GCS and GGS cause pharyngitis. Asymptomatic nose and throat carriage can occur
	Sputum	GCS/GGS pneumonia is uncommon
	HVS	Can cause a vaginal discharge. Can cause vulvitis, perianal cellulitis in pre-pubertal girls. Treatment should be given
	Urine	Very uncommon finding in the urinary tract, and its presence suggests a vaginal source, or in the male, balanitis
	Wound/ulcer swab	Can cause cellulitis and wound infections, including infections in chronic leg ulcers
Streptococcus pneumoniae	Eye swab	Can cause conjunctivitis
	ENT swab	Associated with otitis media and sinusitis. Not a cause of bacterial pharyngitis. Asymptomatic nose and throat carriage can occur
	Sputum	Commonest cause of bacterial pneumonia. Important in COPD
	HVS	When found in association with a discharge, always consider treating. Colonization not recognized
	Urine	Not a cause of UTI
	Wound/ulcer swab	A very uncommon finding in wounds or chronic leg ulcers

(*Continued*)

28

Gram-negative bacteria	Specimen	Comment
Haemophilus influenzae	Eye swab	Can cause conjunctivitis
	ENT swab	Associated with otitis media, sinusitis, and epiglottitis. Asymptomatic nose and throat carriage can occur
	Sputum	A cause of bacterial pneumonia. Important in COPD
	HVS	When found in association with a discharge, treatment should be given. Can cause vulvitis, perianal cellulitis in pre-pubertal girls. Colonization not recognized
	Urine	Not a cause of UTI
	Wound/Ulcer swab	A very uncommon finding in wounds or ulcers
Escherichia coli	Eye swab	Usually considered a colonizer; infection uncommon
(including ESBL producers)	ENT swab	Usually considered a colonizer, but is associated with diffuse otitis externa
	Sputum	When found in a sputum specimen, this usually represents contamination with organisms from the throat that have been selected out by prior antibiotic use
	HVS	Usually considered a colonizer
	Urine	Common cause of UTI
	Wound/ulcer swab	Usually considered a colonizer. Can be one of a mixture of bacteria found, for example in an abdominal wall abscess following surgery
Klebsiella pneumoniae	Eye swab	Usually be considered as a colonizer; infection uncommon
(including ESBL producers)	ENT swab	Usually considered a colonizer, but is associated with diffuse otitis externa
	Sputum	Can be a less common cause of community-acquired pneumonia
	HVS	Usually considered a colonizer
	Urine	Common cause of UTI
	Wound/ulcer swab	Usually a colonizer. Can be one of a mixture of bacteria found, for example, in an abdominal wall abscess following surgery
Proteus	Eye swab	Usually considered as a colonizer
	ENT swab	Usually considered as a colonizer, but is associated with diffuse otitis externa
	Sputum	When found in a sputum specimen, this usually represents contamination with organisms from the throat that have been selected out by prior antibiotic use
	HVS	Usually considered a colonizer
	Sputum	Usually considered a colonizer
	Urine	Common cause of UTI; associated with renal calculi (Always nitrofurantoin resistant!)
	Wound/ulcer swab	Can occasionally cause infections associated with post-operative wounds. Can be one of a mixture of bacteria found, for example, in an abdominal wall abscess following surgery
Pseudomonas	Eye swab	Can cause conjunctivitis, especially associated with contact lens use
	ENT swab	Associated with 'swimmer's' ear, where aural toilet and use of acetic acid/alcohol preparations can resolve the condition. In older diabetic patients, malignant otitis externa is a serious invasive infection, which requires intravenous antibiotics
	Sputum	Associated with infections in bronchiectasis, severe COPD, and cystic fibrosis
	HVS	Usually considered a colonizer

(*Continued*)

28

Gram-negative bacteria	Specimen	Comment
Pseudomonas *(continued)*	Urine	*Pseudomonas aeruginosa* is associated with UTI in individuals with structural abnormalities of the renal tract. It is naturally resistant to many 'front-line' antibiotics, such as amoxicillin, co-amoxiclav, and trimethoprim, and antibiotic use, urinary catheterization favour colonization of the bladder. Pseudomonas is not uncommon in nursing care facilities in the community. It can also be found in the urine of otherwise healthy girls and women, and this may be as a result of heavy, yet transient, introital carriage
	Wound/ulcer swab	Often present as a colonizer, and uncommonly causes infection. Pseudomonas is a recognized cause of folliculitis associated with hot-tubs/whirlpools. Here, the warm water contaminated with pseudomonas is forced into open follicular pores, where it initiates the infection.
Anaerobes	**Specimen**	**Comment**
This group includes: clostridia, anaerobic streptococci, and the gram-negative anaerobes of the mouth such as prevotella and of the bowel, bacteroides. Clinically their presence should be suspected whenever there is a foul smell. For the purpose in the list below, a generic term 'anaerobes' is used		
	Eye swab	Not tested for
	ENT swab	May be associated with chronic sinusitis or mastoiditis
	Sputum	Not tested for
	HVS	Usually considered a colonizer, but can be associated with a bacterial vaginosis. They can also be important in infections following surgery or post-partum, malignancies of the genital tract, and in pelvic inflammatory disease
	Urine	Not associated with UTI
	Wound/ulcer swab	Can be found in post-operative wounds, and abscesses associated with post-partum and gynaecological surgery. In these circumstances, there can be a mixed flora of anaerobes, 'coliforms', and streptococci Anaerobes are usually considered colonizers of chronic leg ulcers, often reported as part of the 'faecal flora'. The ulcer may be foul-smelling, which is the clue to the presence of anaerobes, and is also an indication that the ulcer has progressed to the 'critical colonization' stage (see Chapter 5).
Candida	**Specimen**	**Comment**
Candida are yeasts that are usually minor members of the microbial flora, colonizing moist areas such as the perineum and vagina in low numbers. There are two broad groupings, *Candida albicans*, and the non-*albicans* group such as *Candida glabrata, Candida kruzei*, and *Candida tropicalis*. This differentiation is based on *Candida albicans* being 'germ-tube' positive. *Candida albicans* is usually susceptible to fluconazole		
	Eye swab	Can be associated with keratitis
	ENT swab	Is a minor member of the oral flora, so small numbers are not significant. It causes thrush, which can be found in patients on inhaled steroids, and is important in immunosuppressed cancer patients, and HIV infection
	Sputum	When found in a sputum specimen, this usually represents contamination with organisms from the throat that have been selected out by prior antibacterial use
	HVS	In the asymptomatic patient, a scanty growth is not significant. Overgrowth occurs in circumstances such as oral contraceptive use. Recurrent infection can indicate HIV infection. Can cause balanitis
	Urine	Can be found commonly in the catheterized patient following antibacterial use. Uncommon cause of UTI in the otherwise healthy individual, and when present in urine, it is usually a contaminant from the vaginal flora. Occasionally, the presence in the urine may reflect 'spill over' from a systemic infection
	Wound swab	A wide range of skin conditions are associated with candida, and include paronychia, folliculitis, intertrigo, nappy (diaper) rash, and perianal candidiasis

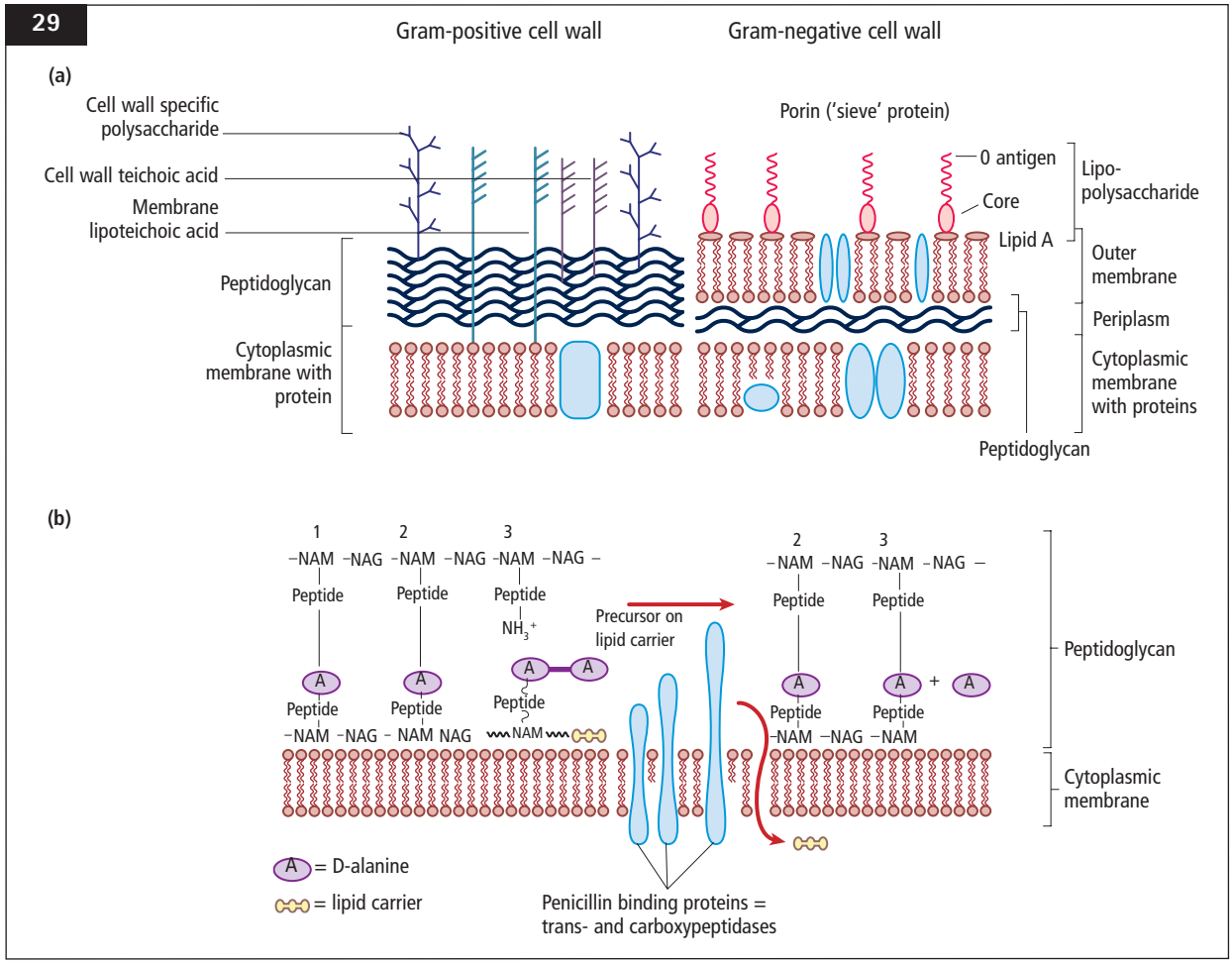
Incorporation of the building block of the peptidoglycan component of the cell wall of bacteria is inhibited by the β-lactam antibiotics (penicillins, cephalosporins, carbapenems), as well as the glycopeptides (**29**).

The site that specific organisms are found at determines their likely clinical significance. In the community setting, *Escherichia coli* is primarily of significance in urinary tract infections (UTIs); it does not cause chest infections or infected ulcers. *Staphylococcus aureus* (methicillin-sensitive *Staphylococcus aureus* [MSSA] and MRSA) causes skin and soft tissue infections, otitis externa, and occasionally UTI, or pneumonia.

While certain organisms are frequently associated with infection at particular sites, a profuse, pure growth of the organism from a site where it would be uncommon, with clear evidence of infection would warrant consideration of treatment. An example is a pure growth of a *Proteus* sp. (a 'coliform') isolated from a post-operation abdominal wound.

THE ACTIVITY OF ANTIBIOTICS AGAINST BACTERIA

A list of the antibiotics discussed in this chapter is shown in **30**. Besides oral agents, topical agents that can be used for infections of the skin and eye are shown. Intravenous agents that can be used in



29 (**a**) The structure of the gram-positive and gram-negative cell wall, and the relationship with the cytoplasmic membrane. Gram-negative bacteria have a periplasmic space bounded externally by the outer lipid membrane. This barrier allows enzymes such as β-lactamases to build up here in high concentration, as a defence against incoming β-lactam antibiotics. β-lactamase enzymes of gram-positive bacteria diffuse through the cell wall and into the surrounding medium. (**b**) The penicillin-binding proteins (PBP) reside in the cytoplasmic membrane, and are responsible for cross-linking the peptidoglycan chain. β-lactam antibiotics bind irreversibly to the active site of these PBP enzymes, destroying their function, and thus the cell.

30

Oral antibiotics

Antibiotic	**Code**	**Class**	
Penicillin	PEN	β-lactam	Penicillin
Amoxicillin	AMO	β-lactam	"
Amoxicillin/clavulanic acid (**Co-amoxiclav**)	COA	β-lactam/inhibitor	"
Flucloxacillin	FLU	β-lactam	"
Dicloxacillin	DIC	β-lactam	"
Cefalexin	CEF	β-lactam	Cephalosporin
Erythromycin	ERY	Macrolide	
Clindamycin	CLI	Lincosamide	
Ciprofloxacin	CIP	Quinolone	
Levofloxacin	LEV	Quinolone	
Moxifloxacin	MOX	Quinolone	
Co-trimoxazole (trimethoprim-sulphamethoxazole)	CoT (**TMP-SMX**)	Sulfonamide	
Metronidazole	MET	Nitroimidazole	
Doxycycline	DOX	Tetracycline	
Rifampicin	RIF	Rifamycin	
Fusidic acid	FUS		
Linezolid	LIN	Oxazolidinone	
Trimethoprim	TRIM		
Nitrofurantoin	NITR	Nitrofuran	

Topical antibiotics

Eye

Chloramphenicol	CHL		
Gentamicin	GENT	Aminoglycoside	
Neomycin	NEO	Aminoglycoside	
Ciprofloxacin	CIP	Quinolone	
Levofloxacin	LEV	Quinolone	
Polymyxin	POLY	Polymyxin	

Skin

Bacitracin	BAC	'Polymyxin-like'	
Fusidic acid (also eye preparation available)	FUS		
Mupirocin	MUP		
Retamapulin	RET	Tricyclic pleuromutilin	

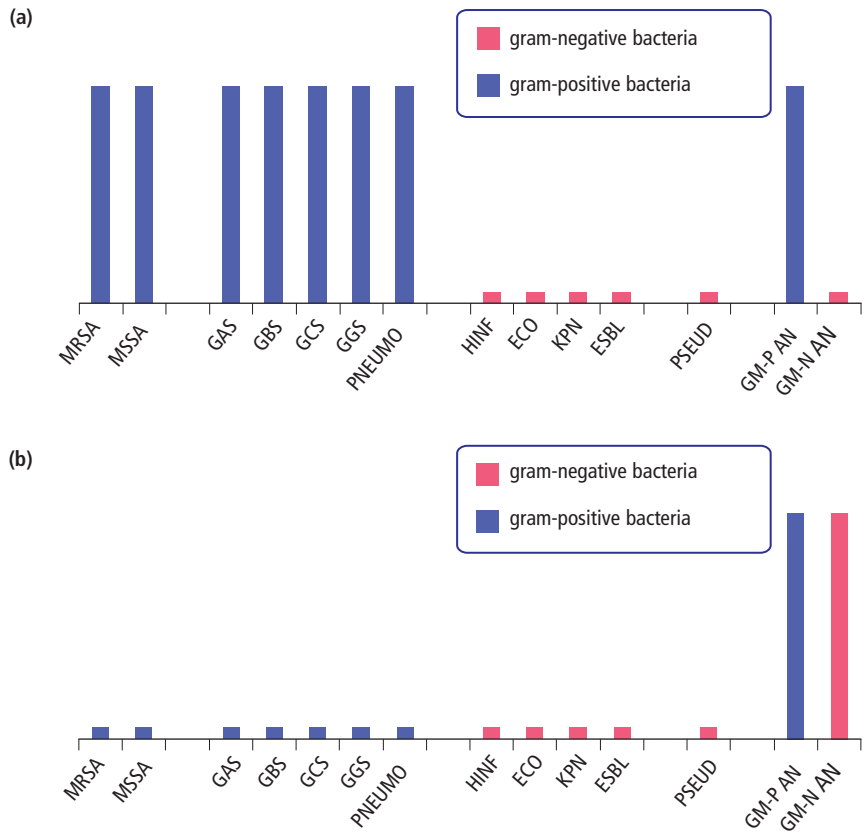
Used in OPAT

Teicoplanin*/(**)	TEIC	Glycopepetide	
Daptomycin	DAP	Glycolipid	
Ceftriaxone	CTX	β-lactam	Cephalosporin
Ertapenem	ERT	β-lactam	Carbapenem
Meropenem***	MER	β-lactam	Carbapenem
Gentamicin****	GENT	Aminoglycoside	

*The first three doses of teicoplanin are given 12 hours apart, and then once daily. (**)Oral teicoplanin (and vancomycin) are not absorbed; they are important agents in the treatment of CDAD. ***Meropenem is usually given 8 hourly, but 3 g doses infused over 30 minutes may be given once-daily.[10] ****Pre-dose gentamicin levels need to be monitored.

30 Antibiotics that can be used in the community, grouped as oral, topical, or intravenous (OPAT) agents. The abbreviated code of each antibiotic is included in the general antibiotic activity diagrams in **33–38**. Further details can be found in more detailed textbooks.[11,12] OPAT: Outpatient parenteral antibiotic therapy

31



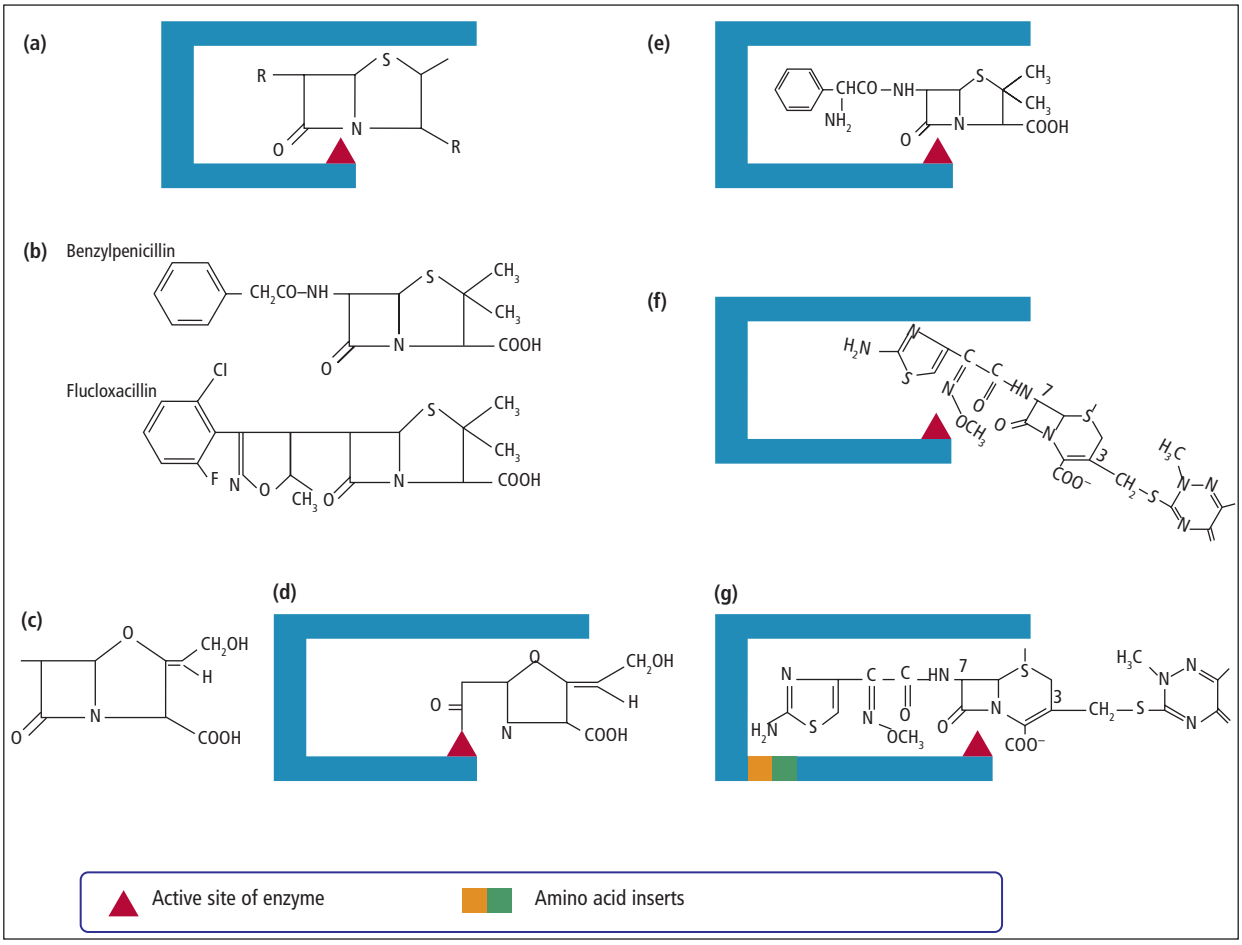
31 The range of activity of (**a**) the glycopeptides (vancomycin and teicoplanin), and (**b**) the imidazole metronidazole. Height of bars represents relative activity.

OPAT are also included. This subject may seem inappropriate in this book; however, with the increase in antibiotic-resistant bacteria causing uncomplicated infections such as cystitis in the community, a hospital admission may be needed if there is no oral option. In such a setting and with an OPAT service in place, the use of parenteral antibiotics with a long half-life can keep these patients out of hospital.

The range of activity of an antibiotic is dependent on a number of factors. Metronidazole for example is effective against obligate anaerobes. This antibiotic probably gets into all bacterial cells at the same concentration. However, only in obligate anaerobes, which have a very negative oxidation-reduction potential, is metronidazole converted to an active radical, that binds to and disrupts the cellular deoxyribonucleic acid (DNA), killing the organism. 'Coliforms' growing anaerobically do not generate a sufficiently negative oxidation-reduction potential to effect the conversion. The glycopeptides vancomycin and teicoplanin are large molecules which diffuse through the peptidogycan cell wall of gram-positive bacteria to reach their site of action. They cannot cross the outer membrane of gram-negative bacteria, and hence lack activity against these bacteria. The distinct range of activity of the glycopeptides and metronidazole is shown in **31**. Further information of the mechanisms of action of antibiotics can be found in more detailed microbiology textbooks.[11,13]

Bacteria are masters at developing resistance to antibiotics, and passing on this resistance profile, which is frequently plasmid mediated, to others. The development of resistance to a wide range of β-lactam antibiotics will always be one of the most significant challenges in treating infections. As soon as a new agent is put into use, bacteria start developing mechanisms to inactivate it, or to bypass

the pathway the antibiotic is inhibiting. β-lactamase-producing bacteria are an example, and include ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae*. In addition to producing β-lactamases, enzymes that inactivate a wide range of penicillins and cephalosporins, these bacteria carry adjacent genes on the plasmid that confers resistance to quinolones (e.g. ciprofloxacin), and aminoglycosides (e.g. gentamicin). (As a generalization, β-lactam/β-lactamase inhibitor combinations such as amoxicillin/clavulanic acid [co-amoxiclav] should be considered to have borderline activity against the ESBL-producing 'coliforms'). The carbapenems, which include ertapenem, imipenem, doripenem, and meropenem are often the only β-lactams that retain activity. Of concern is the emergence of resistance to these antibiotics by a range of carbapenemases.[14] Figure **32** summarizes information on β-lactamases and ESBL-β-lactamases. Further information can be found in more detailed textbooks.[11,13]



32 β-lactams and β-lactamase enzymes. **(a)** The activity of β-lactam antibiotics resides in the C-N bond of the 4-membered β-lactam ring. If this is cut by a β-lactamase enzyme, the antibiotic is inactivated. **(b)** Unlike benzylpenicillin, flucloxacillin has a modified side-chain that sterically prevents it from entering the active site of the β-lactamase produced by *Staphylococcus aureus*. **(c)** Clavulanic acid is a β-lactam that has no antibacterial activity. **(d)** Clavulanic acid binds covalently to the active site of certain β-lactamases such as those of *Staphylococcus aureus, Escherichia coli*, and klebsiella, inactivating them. In combinations of amoxicillin/clavulanic acid (co-amoxiclav), the amoxicillin component thus remains intact to bind to PBP. **(e)** Amoxicillin, on its own, is inactivated by the β-lactamase of *Escherichia coli*. **(f)** Ceftriaxone, with its large R1 residue, cannot enter the active site of the enzyme, and is not inactivated. **(g)** With ESBL-producing *Escherichia coli*, several mutations in the gene coding for the enzyme alter the active site so that it can accommodate ceftriaxone and inactivate it.

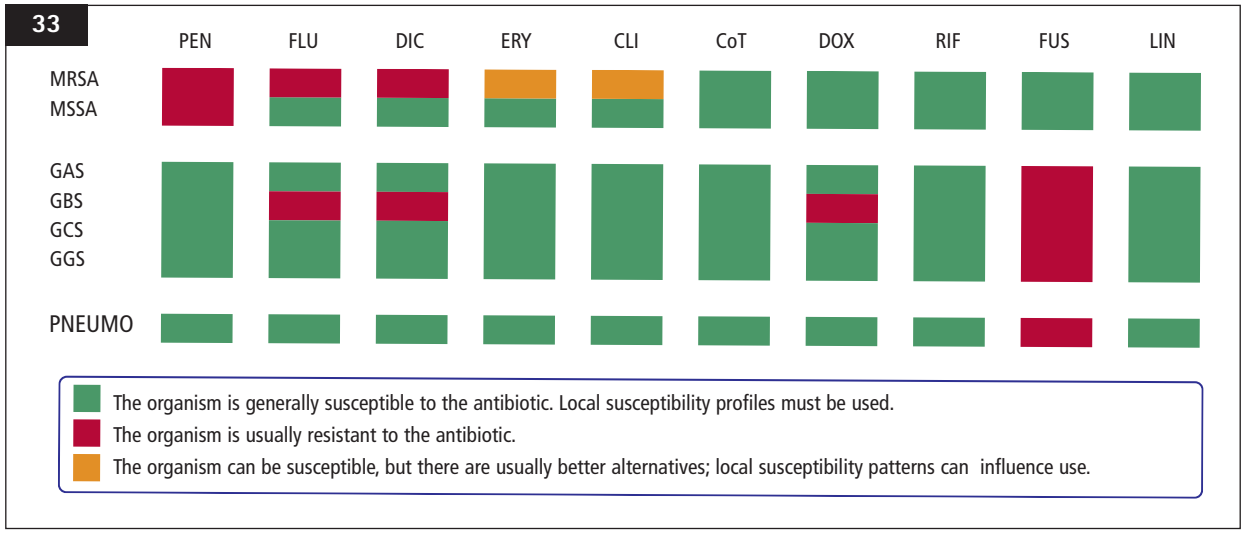
The spectrum of activity of antibiotics listed in **30** is shown in **33–37**. In addition, agents that can be used for OPAT are shown in **38**. These diagrams show the activity of the antibiotic against the bacteria listed in **28**. The activity profiles have been based on information given in detailed texts on antibiotics.[11,12] The 'green' code shows that the organism is always or usually susceptible to the antibiotic, the 'red' code that the organism is always or usually resistant to the antibiotic, and the 'yellow' code shows the organism can be susceptible, but that there may often be better alternatives. The 'purple' code used in **36** and **37** shows the antibiotic is effective when used at high concentration delivered by topical treatment. (For the purpose of this book, these are generalizations for certain antibiotics, and local, regional, and national antibiotic susceptibility profiles must be used in determining which antibiotics to use in clinical guidelines and practice. For example, penicillin-resistant *Streptococcus pneumoniae* is common in certain countries in Europe.)

It is useful to review these figures as the information is relevant in interpreting laboratory reports. Examining the antibiotic susceptibility profile of the haemolytic streptococci A, B, C, G and *Streptococcus pneumoniae* (**33**, **34**) shows them here to be penicillin sensitive. This means that they are also sensitive to amoxicillin, co-amoxiclav, and the cephalosporins. This is important, as laboratories will often only report penicillin, erythromycin, and tetracycline in a wound swab report. If the organism is reported as erythromycin- and tetracycline-resistant, the only option may seem to be penicillin (or amoxicillin). However, if the patient was penicillin allergic, but whose allergy allowed cephalosporins to be given, cefalexin is an option, as penicillin sensitivity equates to cephalosporin sensitivity for these streptococci. Cephalosporins are used less frequently now because of the association with CDAD. However, if the benefit of use is considered to outweigh the risk, an agent such as cefalexin can be considered for an individual patient. This theme is examined in more detail in Chapter 5, **91**. Clearly, the most narrow-spectrum agent that is appropriate should be used to treat infection caused by a particular organism.

ANTIBIOTIC GUIDELINES TO USE IN COMMON INFECTIONS

There has been considerable effort in recent years to ensure that antibiotic guidelines in all health-care settings are developed to minimize the selection of antibiotic-resistant organisms, and reduces the risk of CDAD.[4–7]

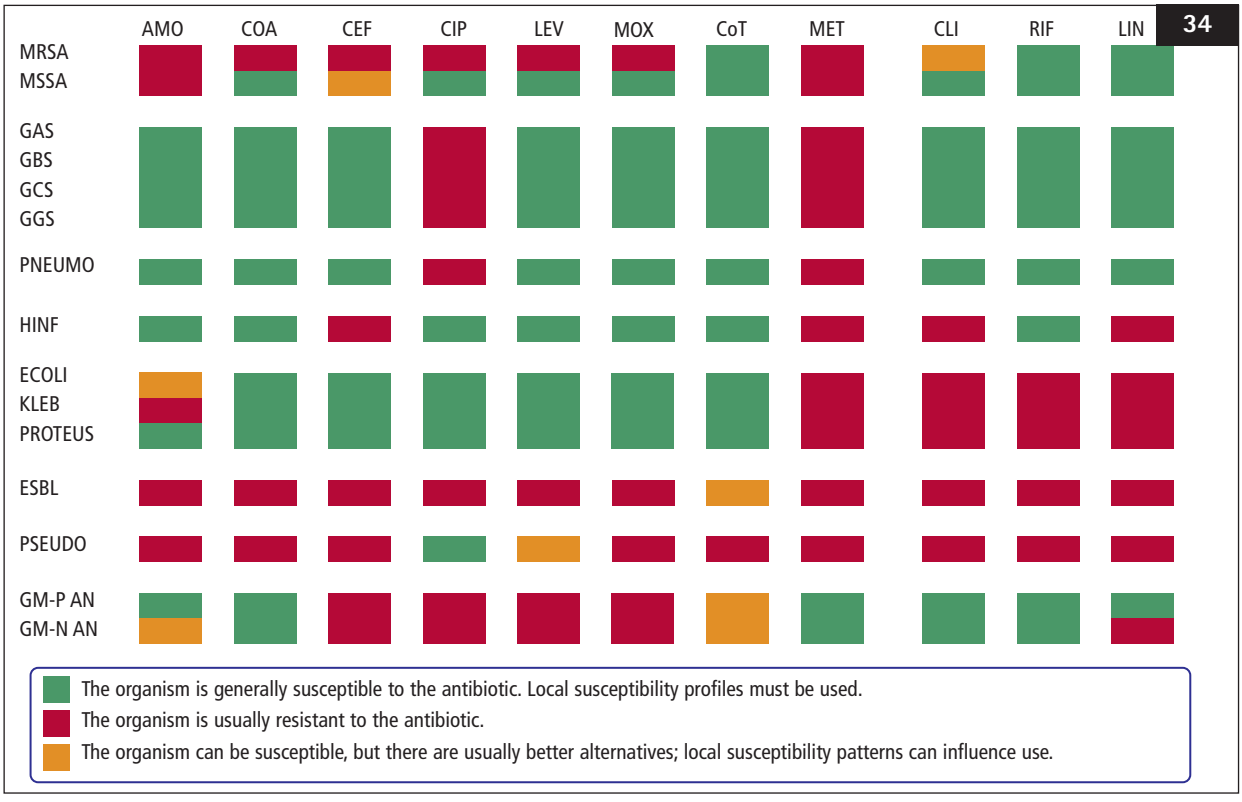
An example of antibiotic guidelines that can be used in the community is given in Chapter 11. These are based on the Community Guidelines originally published by the Health Protection Agency of the UK in 2007. In addition, information



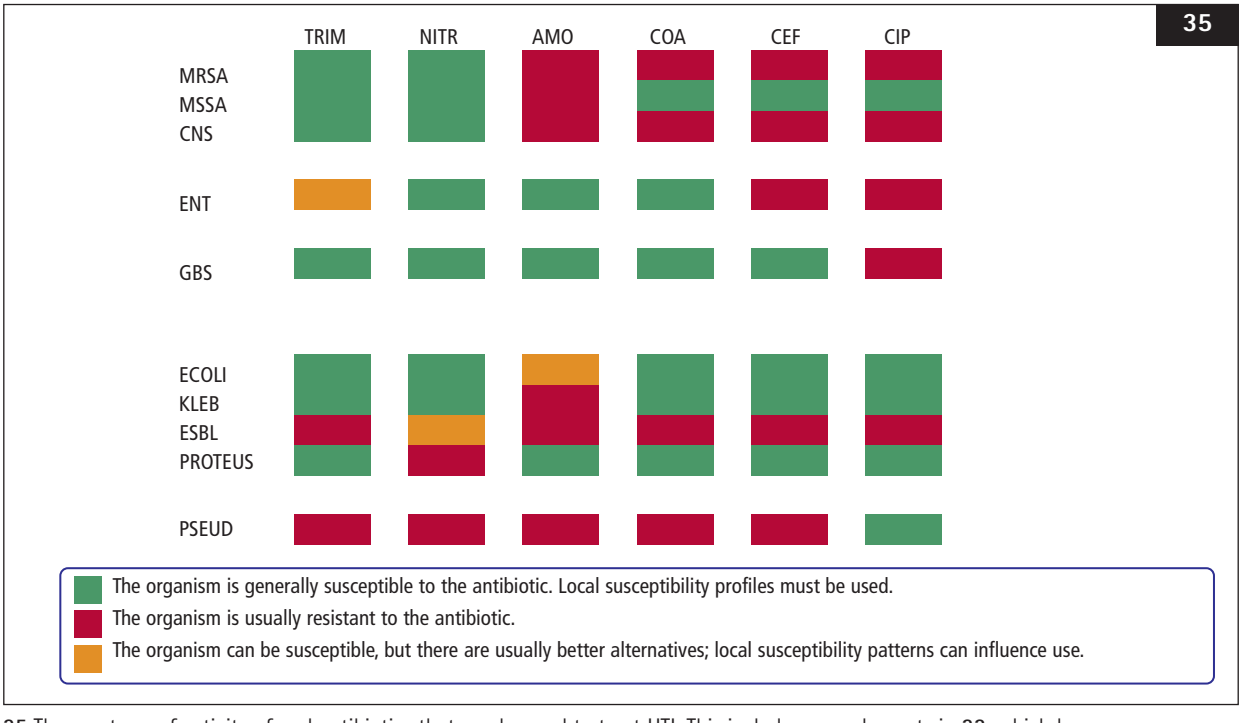
33 The range of activity of some oral antibiotics that can be used in primary care to treat selected gram-positive bacteria. Figures **28** and **30** should be referred to. (For abbreviations, see **30**.)

These are general susceptibility patterns; local laboratory information and guidelines must be used in clinical practice.

- For MSSA and streptococci, susceptibility to clindamycin here is based on the organism being erythromycin sensitive.
- Rifampicin and fusidic acid should not be used as monotherapy, as resistance arises rapidly. They must be used with a second agent, e.g. doxycycline, where appropriate.



34 The spectrum of activity of oral antibiotics that can be used to treat selected gram-positive and gram-negative bacteria. This includes several agents in **33**, which have a wider range of activity. Figures **28** and **30** should be referred to. (For abbreviations, see **30**.)
These are general susceptibility patterns; local laboratory information and guidelines must be used in clinical practice.



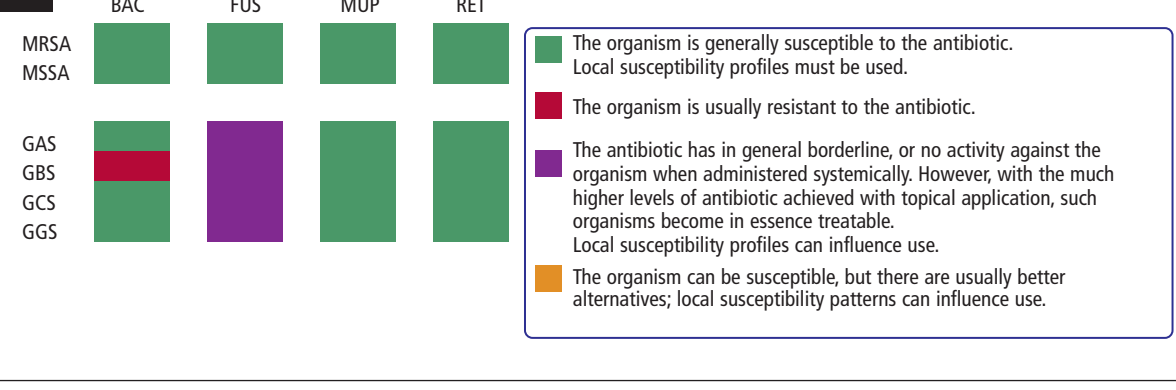
35 The spectrum of activity of oral antibiotics that can be used to treat UTI. This includes several agents in **33**, which have a wider range of activity. Figures **28** and **30** should be referred to. (For abbreviations, see **30**.)
These are general susceptibility patterns; local laboratory information and guidelines must be used in clinical practice.

36

CHL
GENT
NEO
CIP
LEV
POLY
MRSA
MSSA
GAS
GBS
GCS
GGS
PNEUMO
HINF
ECOLI
KLEB
PROTEUS
ESBL
PSEUDO
The organism is generally susceptible to the antibiotic. Local susceptibility profiles must be used.
The organism is usually resistant to the antibiotic.
The antibiotic has in general borderline, or no activity against the organism when administered systemically. However, with the much higher levels of antibiotic achieved with topical application such organisms become in essence treatable. Local susceptibility profiles can influence use.
The organism can be susceptible, but there are usually better alternatives; local susceptibility patterns can influence use.

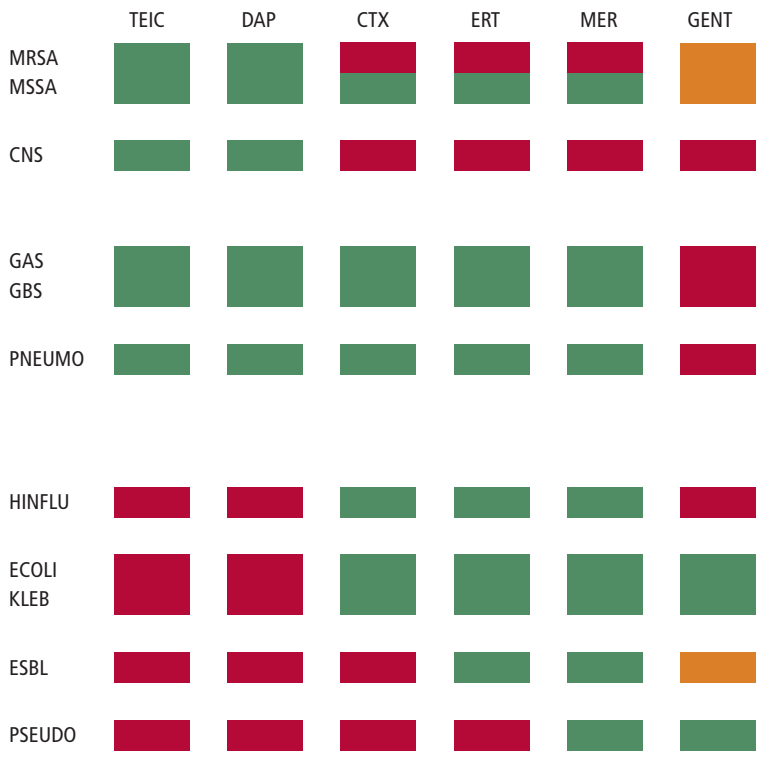
36 The range of activity of selected antibiotics, as topical preparations, that can be used as appropriate, to treat infections of the eye. Figures **28** and **30** should be referred to. (For abbreviations, see **30**.)
These are general susceptibility patterns; local laboratory information and guidelines must be used in clinical practice.

37


BAC
FUS
MUP
RET
MRSA
MSSA
GAS
GBS
GCS
GGS
The organism is generally susceptible to the antibiotic. Local susceptibility profiles must be used.
The organism is usually resistant to the antibiotic.
The antibiotic has in general borderline, or no activity against the organism when administered systemically. However, with the much higher levels of antibiotic achieved with topical application, such organisms become in essence treatable. Local susceptibility profiles can influence use.
The organism can be susceptible, but there are usually better alternatives; local susceptibility patterns can influence use.

37 The range of activity of selected topical antibiotics that can be used to treat infections of the skin. Bacitracin and mupirocin are used to reduce nasal colonization with MRSA. Figures **28** and **30** should be referred to. (For abbreviations, see **30**.)
These are general susceptibility patterns; local laboratory information and guidelines must be used in clinical practice.

38



38 The spectrum of activity of selected intravenous antibiotics that can be used for OPAT. Apart from meropenem, all have pharmacokinetic properties that enable them to be given once-daily. Figures **28** and **30** should be referred to. (For abbreviations, see **30**.) These are general susceptibility patterns; local laboratory information and guidelines must be used in clinical practice.

that would be suitable in the USA is included. Local guidelines must be developed with the local medical microbiology department. The range of activity of an antibiotic, as well as local susceptibility patterns in a particular geographical area should be considered when drawing up these guidelines, which should be reviewed on a regular basis.

Topical antibiotics

The general activity ranges of topical agents for the eye (**36**) and skin (**37**) are shown. Quinolones, such as ciprofloxacin, have in general borderline or no activity against streptococci when administered systemically. However, if applied topically, the much higher concentrations achieved can be sufficient to treat a superficial infection, and for this reason they are used in topical treatment for conjunctivitis. Topical fusidic acid has activity against MSSA and MRSA, and also has activity against streptococci for the same reason. Mupirocin can be used to treat impetigo, and has good activity against MSSA, MRSA, and streptococci. Ratamapulin, a tricyclic pleuromutilin derivative, has a similar range of activity against gram-positive bacteria. Topical antibiotics should not be used for prolonged periods, as resistance is likely to develop, and must not be used for anything other than superficial infections, in formulations made for that purpose.

INTRAVENOUS ANTIBIOTIC USE IN THE COMMUNITY; OUTPATIENT PARENTERAL ANTIBIOTIC THERAPY (OPAT)

Certain intravenous antibiotics started in hospital can be continued in the community as OPAT. An example where this is appropriate is completing the treatment of meningococcal meningitis with 'once-daily' ceftriaxone. The advantage of OPAT is that the patient can be discharged from hospital when it is safe to do so, saving hospital resources, and reducing the risk of hospital-acquired infection to the patient. OPAT requires a service commitment that covers the needs of both the community and hospital to maintain it. In addition to there being an appropriate antibiotic for a particular infection, and having the full management plan in place, each individual patient needs to be assessed to determine if OPAT is suitable. For example, any co-morbidities such as diabetes must be under control, the patient should have good cognitive function or stable mental health, and there should be no logistical barriers (telephone, transport) for using the service.[15] More detailed accounts of using an OPAT service are detailed elsewhere. [16,17]

Nowadays, there are other important reasons for considering the use of OPAT. UTIs caused by ESBL-producing 'coliforms' can be a particular problem in the community, as oral treatment options may be very limited or nonexistent. The patient whose clinical condition does not warrant hospital admission could be offered once-daily ertapenem. Similarly, for treatment of a sensitive ESBL 'coliform' in a patient who recently had protracted CDAD due to *Clostridium difficile*, once-daily gentamicin could be given in the community. This antibiotic is not associated with causing or exacerbating CDAD.[5] Importantly, giving the treatment in the community and not in hospital would remove a further potential exposure to the spores of *Clostridium difficile*.

Teicoplanin and daptomycin are active against gram-positive bacteria, and they can be used in the treatment of cellulitis, prosthetic joint infections, and osteomyelitis in combination with oral antibiotics, when required. While these antibiotics are given by the intravenous route, their pharmacokinetic profiles allow them to be given once daily. The oxazolidinone linezolid, with the same range of activity, is also useful to consider. It can be given both intravenously and by mouth, at a dose of 600 mg twice daily.

Some examples of how OPAT can be used:

- Completion of treatment for meningococcal or pneumococcal meningitis using once-daily ceftriaxone.
- Completion of treatment of complicated orthopaedic infections, e.g. first stage of revision of a total knee replacement (TKR) infected with MRSA. Once-daily intravenous teicoplanin or daptomycin can be considered. (The first three doses of teicoplanin are given 12 hours apart.) A second oral agent is usually given as well.
- Treatment of skin and soft tissue infections using agents such as teicoplanin, daptomycin, or ceftriaxone.
- Treatment of UTI where an ESBL-producing 'coliform' is present, and there is no suitable oral agent. Depending on the susceptibility profile, and history of penicillin allergy, once-daily ertapenem or gentamicin can be used. This would keep the patient out of hospital.

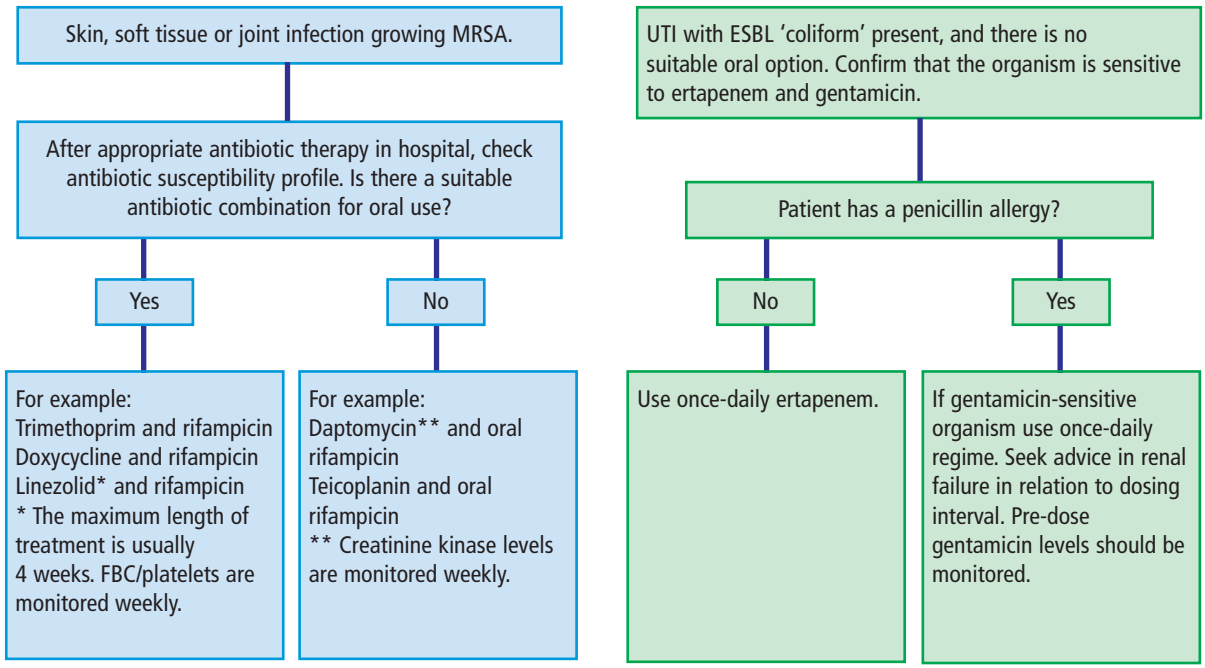
An outline of two examples of OPAT is shown (**39**).

THE ROLE THAT ANTIBIOTICS HAVE IN PREDISPOSING TO *CLOSTRIDIUM DIFFICILE* INFECTION, THE AGENT RESPONSIBLE FOR CDAD

More detailed information about *Clostridium difficile* is given in Chapter 7. The bacterial flora of the body is most complex in the large bowel, and is dominated by a mixture of anaerobes, with smaller, yet essential populations of 'coliforms', streptococci, and enterococci. This bacterial ecosystem provides an environment of 'colonization resistance' that prevents small numbers of pathogens from establishing themselves in sufficient numbers to cause disease. Antibiotic treatment given for a specific infection will cause collateral damage among the organisms making up the 'normal flora' within and without the body. While there is a gradation to the damage caused by an individual antibiotic to this normal flora and the colonization resistance provided, the effect of an individual antibiotic is most pronounced on the fragile ecosystem of the bowel. With the exception of the aminoglycosides such as gentamicin, the majority of antibiotics will have some effect on the bowel flora, and can change the composition to allow *Clostridium difficile* to establish itself. The cephalosporins and quinolones (e.g. ciprofloxacin), and clindamycin are considered to be higher risk agents.[4–8]

The usual source of *Clostridium difficile* is often considered to be in hospital, where environmental contamination may be significant, allowing ready acquisition; carriage rates of about 3% in the community compare with up to 30% in hospital. The use of most broad-spectrum antibiotics leads to derangement of the normal flora of the bowel, and loss of colonization resistance. Once started on antibiotics, the older, debilitated, and malnourished patient is particularly at risk of

39


Skin, soft tissue or joint infection growing MRSA.
After appropriate antibiotic therapy in hospital, check antibiotic susceptibility profile. Is there a suitable antibiotic combination for oral use?
Yes
No
For example:
Trimethoprim and rifampicin
Doxycycline and rifampicin
Linezolid* and rifampicin
* The maximum length of treatment is usually 4 weeks. FBC/platelets are monitored weekly.
For example:
Daptomycin** and oral rifampicin
Teicoplanin and oral rifampicin
** Creatinine kinase levels are monitored weekly.
UTI with ESBL 'coliform' present, and there is no suitable oral option. Confirm that the organism is sensitive to ertapenem and gentamicin.
Patient has a penicillin allergy?
No
Yes
Use once-daily ertapenem.
If gentamicin-sensitive organism use once-daily regime. Seek advice in renal failure in relation to dosing interval. Pre-dose gentamicin levels should be monitored.

39 Two examples outlining the ways that oral and/or intravenous antibiotic therapy can be used in the community.

developing CDAD. However, poor antibiotic husbandry in the community means that the bowel flora may be already disrupted, and the patient is 'primed' to be at risk of *Clostridium difficile* infection prior to hospital admission. *Clostridium difficile* can be acquired in the community, emphasizing the risk associated with antibiotic use there as well.[9] Cases occur in the community in patients who have had no association with a hospital or other medical setting.

Reduction in antibiotic use, as well as the classes of antibiotics prescribed is an essential part in controlling CDAD. If the individual patient is infected with an antibiotic-resistant organism, there is usually an effective treatment option. CDAD may be considered more serious, as it condemns the patient to a potentially life-threatening, yet preventable illness.

THE EXPECTATIONS OF PATIENTS AND PARENTS

In the UK, for example, upper and lower respiratory tract infections, pharyngitis, and otitis media account for over 40% of the clinical indications for which antibiotics are prescribed in the community; UTI and genital tract infections account for less than 10% and 1%, respectively. The main antibiotic prescribed is amoxicillin (25%), with erythromycin, flucloxacillin, trimethoprim, and penicillin V accounting for about 7–8% each of total use.[18]

The *Drug and Therapeutics Bulletin* (DTB) of April 2007 addresses the problem of inappropriate antibiotic use and states that reducing excessive and inappropriate use of antibacterials is key to tackling the global problem of increasing prevalence of antibiotic-resistant organisms.[19] The DTB Editorial also states that patients rarely make explicit requests for antibacterials, and their expectations are not normally discussed at consultation. Patient satisfaction correlates better with information and reassurance rather than receipt of an antibacterial prescription. For the parents of a sick child, reassurance after careful assessment is important. The absence of vomiting and fever in a child presenting with acute otitis media helps reduce the need for antibiotics. Prescribing antibacterial therapy immediately for patients presenting with a sore throat increases future consultations for sore throat by 'medicalization' of the condition.

In addition, prior attendance with upper respiratory tract infection (URTI) increases future re-attendance with sore throat.

The key to reducing antibiotic use in primary care is reduction in the number of consultations for URTI. In addressing this, public awareness is important, and it is likely that patient information sheets do contribute to self-management of common illnesses, including URTI.

These points emphasize again the power of the laboratory report. The presence of an organism together with its antibiotic susceptibility profile is rarely sufficient information alone to initiate antibiotic therapy, and must not be used solely to determine antibiotic prescription. It is the full assessment and review of the patient that should determine the need for an antibiotic.

Mechanisms to reduce antibiotic use

Delayed antibacterial prescribing

For URTI, an antibacterial prescription can be given, and only used when symptoms worsen. Asking the patient to return to the practice/clinic to collect the prescription is associated with a greater decrease in antibacterial use than providing a prescription with instructions not to collect the antibacterial immediately. The DTB review cites one study of children with otitis media that showed reduction in symptoms with immediate antibacterial treatment was modest (a 1-day reduction in symptom duration and reduced use of paracetamol), and was offset by an increased frequency of diarrhoea.

The use of short antibacterial courses

Evidence now shows that in several clinical situations, a short course of antibacterial treatment is as effective as a longer course.[20] For cystitis in otherwise healthy women, a 3-day course of antibiotics is appropriate. In uncomplicated UTI in children, it has been shown that 2–4 days of treatment is as effective as 7–14 days.[21] For URTI, including otitis media, a 5–7 day course should generally be used.[22]

SUMMARY AND KEY POINTS

As shown in Chapter 1, **6**, urine specimens account for about 60% of all specimens received in bacteriology from primary care, reflecting the burden of UTI in the community, especially in women between the ages of 20 and 50 years. The question is can the work generated by all these specimens be more targeted to make the process more cost effective, while at the same time benefiting the patient? Women with UTI have indicated that they do want to avoid taking antibiotics, and thus the unwanted side-effects associated with their use.[23] A cost-effective approach to managing uncomplicated UTI in women in the community could involve immediate antibiotic prescription based on dipstick testing, or empirical delayed prescription, with the patient being fully involved in the management decision.[24] Delayed prescription can reassure patients, and validate their experience of their own symptoms, and their reason for visiting the primary care physician on each occasion.[23, 24]

A more managed approach to antibiotic prescription, involving the patient has the potential to reduce antibiotic use. Such an approach needs to work in parallel with the reason for taking a urine specimen for examination. This sets the theme for the remaining chapters, which emphasize the importance of considering the reason for taking every specimen, and once that decision is made, the quality of specimen collection and interpretation of the report.

In summary, the following points should be noted:

- That relatively few bacterial species cause the majority of infections in the community. It is important to appreciate the key features of these organisms, and the activity that various antibiotics have against them.
- While certain bacteria would always be treated when reported by the laboratory, for example group A streptococcus, others such as *Staphylococcus aureus*, *Escherichia coli*, and group B streptococcus can cause specific diseases, but are also found as ‘colonizers’. It is important to appreciate the circumstances when an organism is acting as a pathogen or non-pathogen, and the differences between colonization and infection.

3
The Urine Specimen

- Introduction
- Organisms and epidemiology
- Specific issues relating to the urine specimen
- Primary care
- The patient
- Collecting the urine specimen
- The request form
- The laboratory report
- Sterile pyuria
- Treatment
- Summary and key points

INTRODUCTION

Urine specimens are the commonest specimen submitted to the microbiology laboratory from primary care, accounting for approximately 60% of the workload received. Given this fact, it is surprising how often the whole process is mismanaged. There are a number of pitfalls in the process from deciding when to take a specimen through to prescribing antibiotic therapy.

The three key points to consider when considering submitting a urine specimen for microbiology investigation are:

1. **Knowing when to collect a urine specimen:** Asymptomatic bacteriuria is common over the age of 65 years and there is no evidence that antibiotic therapy is indicated for this condition. Although it may seem relatively innocuous taking a specimen when there is no clinical evidence of infection, this can set in motion a chain of events resulting in at the least a waste of resources through to unnecessary antibiotic therapy, which may lead to complications in the patient.
2. **Ensuring that a good quality specimen is collected:** Are patients provided with written information on how to collect a specimen? Do the primary care staff expect the female patient to be able to pass urine directly into a narrow container? Contaminated specimens are common, particularly in the female patient. A useful exercise would be to see how many urine reports either come back as a mixed growth or contain significant numbers of epithelial cells, markers for a poorly collected specimen. Laboratory experience shows that a considerable proportion of urine specimens are contaminated.
3. **Knowing how to interpret the laboratory report:** Patients are treated unnecessarily and urine specimens often repeated for no good reason because the report has not been interpreted correctly. Interpretation is far easier if time is invested in collecting the specimen correctly in the first instance.

Figure **40** and the Quick Action Guides expand on these issues, and can be used as a training tool to emphasize the critical steps relevant to practice in primary care.

40 The urine specimen; an example of the consequences of taking a specimen when there is no clinical indication. The steps in the process can be divided into seven critical steps (see Chapter 1, 1).

In this scenario, critical step 1 is breached, as there was no need to send a urine from an otherwise well 75-year-old female patient, who is in an age group where asymptomatic bacteriuria is common. A trace of protein and blood, NOT indicators of UTI, incorrectly directs the primary care staff to send the urine to the laboratory for MC & S. Critical step 2 is breached as the patient is given no information on how to minimize contamination or the correct receptacle for collecting the specimen. The fact that the final culture report shows moderate numbers of epithelial cells and a mixed growth, is indicative of poor specimen collection. Critical step 7 is also breached, when the primary care physician is asked by the nurse to act on the laboratory report. The physician does not review the reasons for collecting the specimen, and is influenced by the culture report and antibiotic susceptibility profile, referring the patient to hospital for intravenous antibiotics. Discussion between hospital medical staff determines there is no need for treatment; the patient is sent home.

Storing and transport of the urine specimen

Urine is a good culture medium for bacteria, and they will multiply in urine that is incorrectly stored. Urine specimens should be transported promptly to the laboratory for processing. If there is a delay, the specimen must be refrigerated in the designated practice/clinic refrigerator to arrest bacterial growth; this is suitable for up to 48 hours, but WBC, RBC, and epithelial cells deteriorate after 24 hours.

Specimen containers with boric acid should preferably be used, which 'preserve' bacterial numbers for up to 72 hours. It is important that the container is filled to the mark in order to achieve the correct boric acid concentration (final concentration 1.8% w/v). The container should then be inverted several times to dissolve the boric acid. Specimens can be stored refrigerated if there is a delay in transport. In the laboratory, the 'plating-out' process dilutes the boric acid to subinhibitory concentrations.

If there is insufficient urine to fill to the mark on a boric acid container, e.g. a urine sample from children, a sterile white-topped container without boric acid must be used, as higher concentrations of boric acid kill certain bacteria. This specimen must be refrigerated if there is any delay in transport.

40

CRITICAL STEP 1:
Is collection of a specimen indicated?

The primary care team decides to collect a 'routine' urine specimen from an asymptomatic 75-year-old diabetic patient who has come for blood glucose monitoring. Urine dipstick, shows '+ protein, +blood'. This is sent to Microbiology for MC & S.

CRITICAL STEP 2:
Obtain a good quality specimen.

The patient is given a sterile universal container but no advice about collecting a MSU.

CRITICAL STEP 3:

Record the full patient and clinical details and type of specimen on the request form. Where necessary, record the specific test request.

CRITICAL STEP 4:

How is the specimen stored and what is the frequency of transport to the laboratory?

CRITICAL STEP 5:

What is the quality of the laboratory process, including turnaround times?

CRITICAL STEP 6:

Is immediate or routine reporting of this result required by the laboratory?

CRITICAL STEP 7:
How is the laboratory report interpreted?

Report on AB, 75-year-old. Urine MC&S:

WBC: 23 x 10^6/L
RBC: 20 x 10^6/L
Epithelial cells: Moderate numbers present

Mixed growth including *Klebsiella pneumoniae* >10^8 colonies/L. This is an ESBL producer.

Resistant to amoxicillin, co-amoxiclav, cefalexin, ciprofloxacin, nitrofurantoin, trimethoprim.

Sensitive to gentamicin, ertapenem, meropenem.

The primary care physician is asked to review the report, and noting that there are no oral alternatives to treat the ESBL-producing *Klebsiella pneumoniae*, decides to refer the patient to hospital for intravenous antibiotics.

The ED physician reviews the MSU result with the Medical Microbiologist. This shows relatively few WBC. There are a moderate number of epithelial cells, showing a contaminated specimen, confirmed by the mixed growth of bacteria. Most importantly the patient is asymptomatic; there is no need for admission and intravenous antibiotics. The patient is sent home.

Quick Action Guide

The flow diagrams below outline the steps to take when considering the need to collect a MSU specimen for dipstick and possible culture.

(Adapted from *Diagnosis of UTI; Quick Reference Guide for Primary Care*. www.hpa.org.uk).[1] With permission of the UK Health Protection Agency.)

DOES THE PATIENT HAVE SYMPTOMS OF A UTI?
For children (<13 years) go to **60** and **61**.

- Local symptoms: Dysuria, frequency, urgency, polyuria, suprapubic tenderness, renal angle tenderness.
- The older patient (>65 years): Signs of infection are dysuria, new incontinence, pyrexia, new or increased confusion, loss of diabetic control (usually consider specimen collection if two or more of these symptoms/signs).[2]
- For the catheterized patient, systemic symptoms are relevant, and include pyrexia >38ºC, hypotension, new or increased confusion, loss of diabetic control.

NO

Do not investigate for a UTI further (Asymptomatic bacteriuria in pregnancy, the renal transplant patient, and screening before urological procedures are exceptions).

YES

Go to the next page

Common causes of inappropriate investigation and treatment

- Apart from the need to screen in pregnancy, the renal transplant patient, and before urological procedures, screening for asymptomatic bacteriuria is not necessary.
- Asymptomatic bacteriuria is a common finding in the age group of +60 years, and there is no benefit in diagnosing and treating the condition. Unnecessary treatment can potentially harm the patient, and wastes money. *DO NOT SEND A SPECIMEN.*
- In the setting of vague symptoms, a dipstick test that only shows the presence of protein and/or blood is not diagnostic of a UTI. *DO NOT SEND A SPECIMEN.*
- Bacteriuria is an inevitable consequence of long-term (>5 days) catheterization. *UNLESS THE PATIENT HAS SYMPTOMS OF INFECTION DO NOT SEND A SPECIMEN.*

Quick Action Guide

The patient is symptomatic
(For children <13 years, see **60** and **61**).

Non pregnant, sexually active female (13–50 years), with 'first episode' of acute cystitis, with clear symptoms of a UTI. ⚠

Three or more of dysuria, frequency, urgency, polyuria, suprapubic tenderness.

No vaginal discharge or irritation.

Acute uncomplicated UTI.

Consider empirical antibiotic treatment (3-day course).

All other patients: Collect a MSU (or CSU).

Give patient specimen collection pack and written information on how to collect specimen. Inform patient about need to fill to the line of a boric acid container, if used.

Female patient, not fitting the criteria of ⚠**, go to the next page.**

Male patient: (Do dipstick). Specimen should be sent to the laboratory and give empirical treatment for 7 days.

CSU: (No dipstick). Send specimen to the laboratory. Give empirical treatment.

The urine dipstick is a 'near patient test.' Practices/clinics must have training programmes for this. The test must be done on a MSU.

Nitrite is produced by bacteria multiplying in the bladder, and although often impractical, the first urine of the day is likely to be the most representative of the infection process in the bladder.

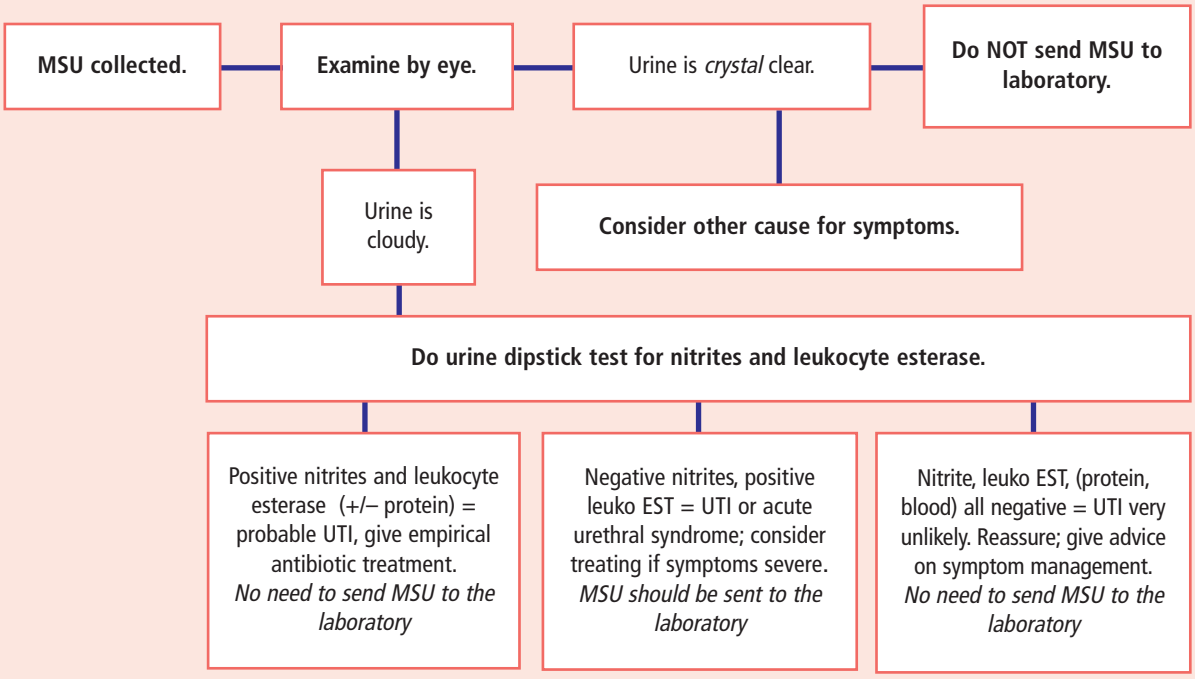
High fluid intake with frequent micturition can dilute nitrites in the urine.

Leukocytes represent the inflammatory response, and the leukocyte esterase of intact and lysed leukocytes is measured.

Red cells and protein can be found in UTI, but are also present in other conditions; when these alone are detected, consider an alternative diagnosis.

Quick Action Guide

Female patient, with 'mild' UTI or two or more symptoms of dysuria, frequency, urgency, polyuria, suprapubic tenderness. In the elderly patient: fever, new or increased confusion, loss of diabetic control are also relevant symptoms. Use this guide in conjunction with BOX A (below).


MSU collected.
Examine by eye.
Urine is *crystal* clear.
Do NOT send MSU to laboratory.
Urine is cloudy.
Consider other cause for symptoms.
Do urine dipstick test for nitrites and leukocyte esterase.
Positive nitrites and leukocyte esterase (+/– protein) = probable UTI, give empirical antibiotic treatment. *No need to send MSU to the laboratory*
Negative nitrites, positive leuko EST = UTI or acute urethral syndrome; consider treating if symptoms severe. *MSU should be sent to the laboratory*
Nitrite, leuko EST, (protein, blood) all negative = UTI very unlikely. Reassure; give advice on symptom management. *No need to send MSU to the laboratory*

Always review the need to send a MSU or CSU based on criteria in BOX A.

BOX A: MSU should be sent to the laboratory (do dipstick as well) when:

- Recurrent UTI (>2/year)
- Resistant bacteria possible
- Persistent symptoms
- Failed treatment
- Abnormal renal tract
- Renal impairment
- Suspected pyelonephritis
- Pregnancy

ORGANISMS AND EPIDEMIOLOGY

A list of common organisms that cause urinary tract infection (UTI) in the community is given in **41**. The majority of infections (>85%) are caused by the 'coliforms', and uropathogenic strains of *Escherichia coli* in particular.[3,4] In females, uropathogenic *Escherichia coli* adheres to and colonizes the introitus in large numbers, from where it can reach the bladder.[4] Binding to the epithelium reduces the likelihood that it will be flushed out at micturition, thereby establishing a 'foothold'. The physiological and immune defences of the bladder may evict the bacteria, but if this cannot be done, cystitis is established. *Proteus* spp. are associated with the formation of renal calculi in alkaline urine, and are inherently resistant to nitrofurantoin. The antibiotic susceptibility pattern of the bacteria ranges from those fully sensitive to the antibiotics tested through to those for which there is no oral option such as extended-spectrum β-lactamase-(ESBL) producing *Escherichia coli* and *Klebsiella pneumoniae*. Laboratories can produce data showing the relative activity of the common antibiotics used to treat UTIs against organisms isolated locally. Such information needs to be interpreted with caution. There is overrepresentation from patients with recurrent UTI as specimens are almost always submitted in this situation. These specimens can harbour antibiotic resistant organisms. Conversely, young female adults presenting with their first UTI are often treated empirically without submitting a urine specimen. Organisms isolated from such individuals are often sensitive to a wider range of antibiotics. Hence the data produced by the laboratory are a composite sensitivity pattern and do not necessarily relate to any particular patient group. If such data are to be used, one must make an assessment of each individual patient. For example, the patient presenting with their first UTI and no previous antibiotic history is likely to have an infection with a much more sensitive organism.

Pseudomonas aeruginosa can be a difficult organism both to interpret its significance and treat. It is naturally resistant to many 'front-line' antibiotics such as amoxicillin, co-amoxiclav,

41

	Antibiotic problems	Comment
Gram-negative		
Escherichia coli	ESBL-producers	There is often no oral option for treating 'ESBL coliforms'
Klebsiella spp.	ESBL-producers	There is often no oral option for treating 'ESBL coliforms'
Proteus spp.		Associated with renal calculi; resistant to nitrofurantoin
'Coliforms'		
Pseudomonas aeruginosa	Ciprofloxacin resistance	Associated with UTI in care homes, previous antibiotic use, and in catheterized patients. If clear symptoms of a UTI, consider treating, noting that quinolones are the only oral option, and CDAD is thus a risk. If not, a repeat clean-catch MSU should be collected. (See Chapter **2** and **28**)
Gram-positive		
Group B streptococcus (GBS)		Note relevance to neonatal sepsis and meningitis; a GBS UTI in pregnancy should be clearly recorded in the patient's records
Enterococci	GRE	GRE are glycopeptide-resistant enterococci Enterococci are inherently resistant to cephalosporins
Coagulase-negative staphylococcus (CNS)		
Staphylococcus saprophyticus		Associated with UTI in young sexually active females
Staphylococcus aureus (MSSA)	MRSA	Uncommon cause of UTI in the patient without an indwelling urinary catheter. Can be relevant in the patient who has had recent instrumentation of the bladder. The organism can also reach the urinary tract from the blood via a bacteraemia. A spinal collection or endocarditis can be sources of this

41 A list of more common bacteria that cause UTI. All culture reports should be interpreted in conjunction with the clinical details, and the result of the urine microscopy in order to confirm the significance.

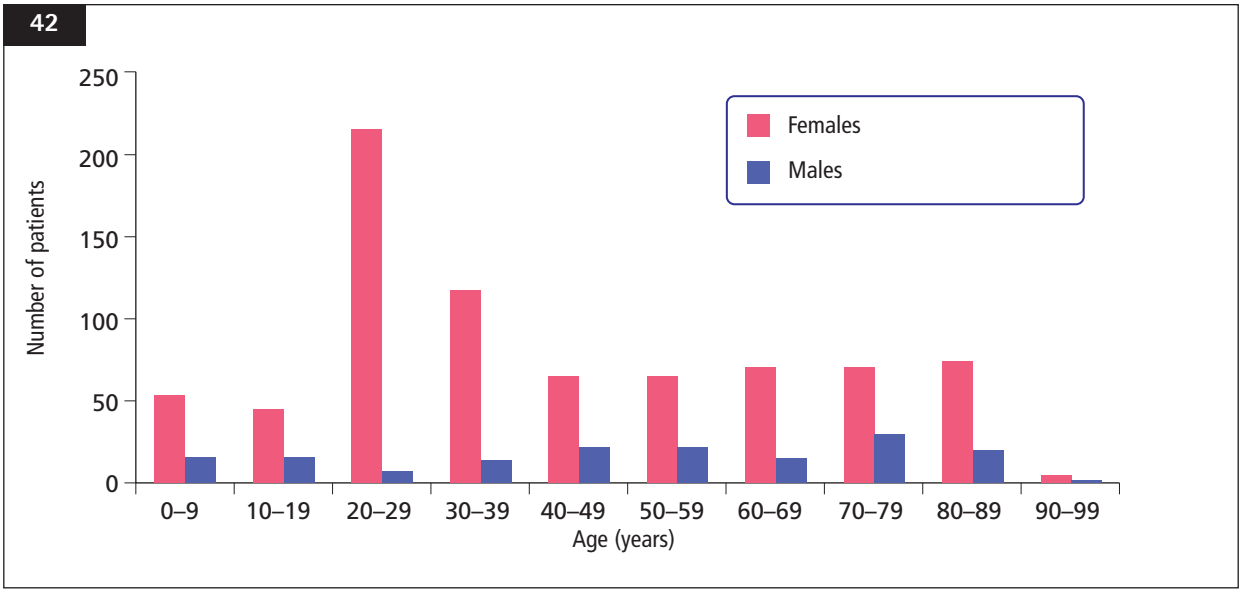
nitrofurantoin, and trimethoprim. Antibiotic use, as well as urinary catheterization, favour colonization of the bladder; pseudomonas is not uncommon in nursing care facilities in the community for these reasons. It is also associated with complications such as obstruction due to a stone, the presence of a stent, or following instrumentation or surgery of the urinary tract.[5] While a definite UTI with pseudomonas, based on symptoms and a confirmatory midstream urine (MSU) report warrants treatment being considered, if there is any doubt, the patient should be reviewed, and a repeat MSU collected. Not infrequently when no treatment is given, a repeat specimen shows that the pseudomonas is no longer present. Pseudomonas can occasionally be found in the urine of otherwise healthy girls and women, and this may be as a result of heavy, yet transient, introital colonization. The organism is an aerobe, and it has difficulty metabolizing at a pH much below neutrality, and transient acidification may remove it from the bladder. Treatment with a quinolone, such as ciprofloxacin (or fosfomycin if available), is the only oral option in the community setting, and the risk of *Clostridium difficile*-associated diarrhoea (CDAD) needs to be taken into account.

The presence of candida in urine is not uncommon, and usually does not indicate a UTI.[6] In the otherwise healthy female, its presence most likely reflects contamination of a urine specimen with vaginal secretions. Candida is found in the urine of the catheterized patient, reflecting previous or current use of antibacterials. If candida is isolated repeatedly from the MSU of the noncatheterized individual, this warrants investigation; it is appropriate to contact the medical microbiologist/infectious diseases physician.

Urine is the main specimen type submitted to the laboratory from primary care, accounting for about 60% of all bacteriology specimens received (Chapter 1). When several hundred consecutive specimens are collated on the basis of the age and sex of the patient, this shows that UTI primarily affects females; about 20% of specimens come from males (**42**). Females in the age group 20–39 years account for over 40% of the specimens submitted, probably reflecting the relationship between sexual activity and UTI in this group.[7, 8] Approximately 30% of urine specimens are from women over the age of 60 years. Examining the clinical details on request forms from this group shows that many specimens are collected for doubtful reasons, such as 'routine examination', 'urine cloudy', or '+blood, ++protein' on dipstick testing. Asymptomatic bacteriuria is common in the older patient, and specimens should not be sent unless there is evidence of infection.

UTI is rare in men less than 50 years of age.[9] The sexually active male with dysuria should prompt the possibility of a sexually transmitted infection (STI), which can present with symptoms similar to a UTI. The most common causes of urethritis are chlamydia and *Neisseria gonorrhoeae* which do not grow on the routine medium used for

42



42 The typical age and sex distribution of patients submitting urine specimens during 1 week to the laboratory.

culturing urine. A laboratory report showing a sterile pyuria in such a patient should prompt consideration of a STI (see Chapter 4).

In uncircumcised males, and young boys in particular, a urine specimen may be contaminated with group A streptococcus (GAS) that is causing balanitis; this condition should be checked for. The finding of GAS in the urine of a young girl almost invariably reflects contamination of the urine with vaginal secretions. In such situations where the GAS is a urinary contaminant from surrounding infected tissues, antibiotic therapy should be modified accordingly. Thus, treatment with a penicillin or a macrolide is justified. Even if reported as sensitive, nitrofurantoin should not be used as it is a urinary antiseptic and does not achieve sufficient levels in tissues to be active. (Note that erythromycin is not indicated for the treatment of UTI.)

A summary of the prevalence of UTI on the different ages of life is shown in **43**.

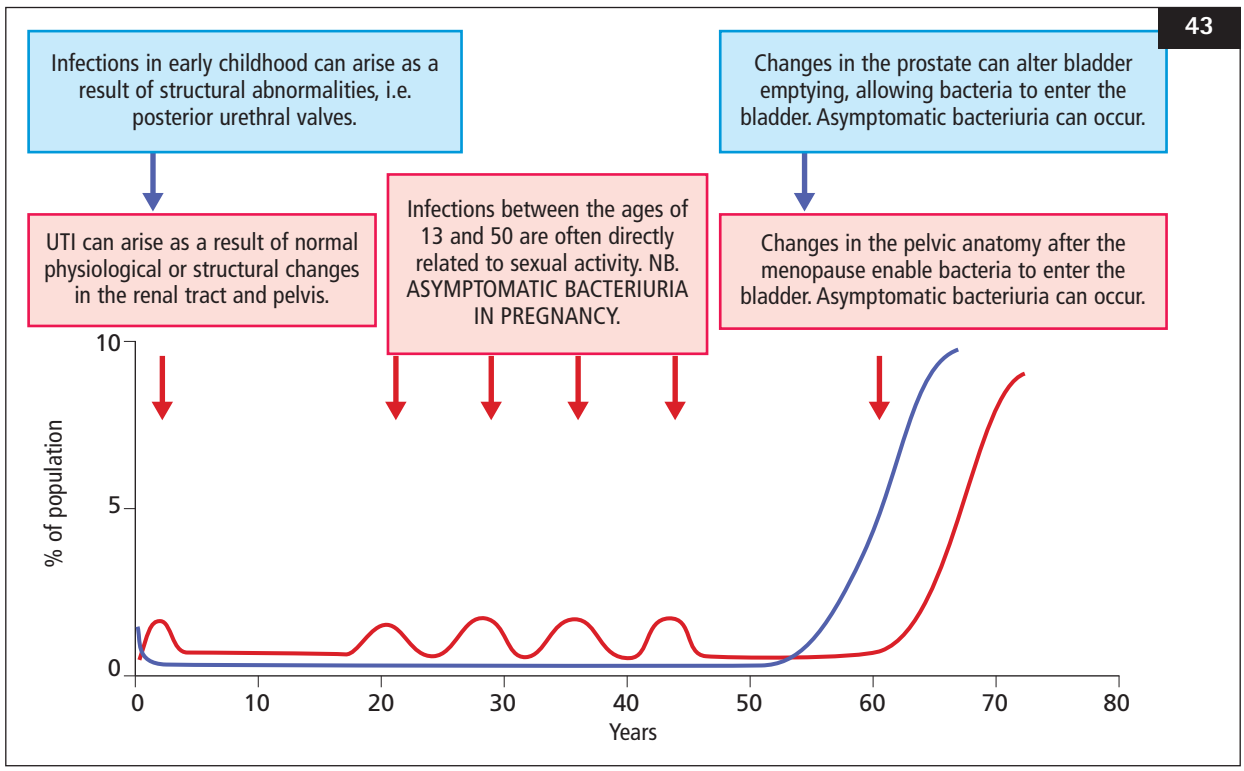
SPECIFIC ISSUES RELATING TO THE URINE SPECIMEN

Anatomical considerations

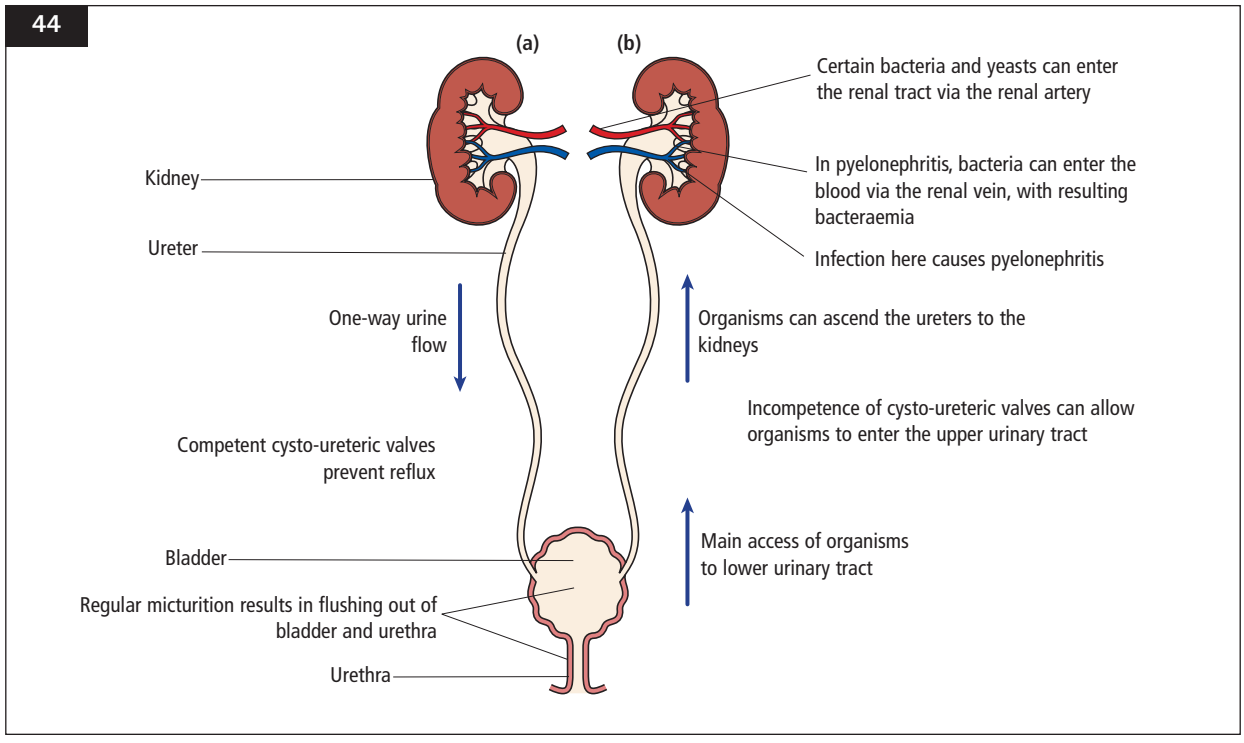
UTI occurs when bacteria exploit anatomical and physiological features of the urinary tract. The female is at a disadvantage, as the short urethra makes it easier for bacteria to reach the bladder (**44**, page 54). Any interference with complete bladder emptying will predispose the individual to colonization. This includes hypertrophy of the prostate, and compromise to the innervation of the bladder and its sphincters in the diabetic.

Uncomplicated and complicated UTI

UTI can be classified as uncomplicated or complicated. The latter includes infection with resistant bacteria, failed antibiotic treatment or persistent symptoms, pyelonephritis (except in otherwise healthy females), and infections associated with functional, metabolic, or anatomic abnormalities of the renal tract, and renal impairment.[10, 11] The clinical spectrum ranges from mild cystitis to life-threatening urosepsis.[11] A urine should always be sent to the laboratory for examination in complicated infections.[1] By definition, a relapse refers to recurrent infection with the same organism, usually within 2 weeks of completing treatment. Here, an occult source of infection, which can be associated with a urological abnormality, should be excluded. Reinfection refers to recurrent infection, often with a different strain or species. This is usually more than 2 weeks after completion of therapy. Recurrent infections


43
Infections in early childhood can arise as a result of structural abnormalities, i.e. posterior urethral valves.
Changes in the prostate can alter bladder emptying, allowing bacteria to enter the bladder. Asymptomatic bacteriuria can occur.
UTI can arise as a result of normal physiological or structural changes in the renal tract and pelvis.
Infections between the ages of 13 and 50 are often directly related to sexual activity. NB. ASYMPTOMATIC BACTERIURIA IN PREGNANCY.
Changes in the pelvic anatomy after the menopause enable bacteria to enter the bladder. Asymptomatic bacteriuria can occur.
% of population
10
5
0
0
10
20
30
40
50
60
70
80
Years

43 The prevalence of bacteriuria in percent, in males (blue) and females (pink) in the stages of life. Note that asymptomatic bacteriuria is a common finding in the patient over 65 years, and there is no benefit in treating this.


44
(a)
(b)
Certain bacteria and yeasts can enter the renal tract via the renal artery
Kidney
In pyelonephritis, bacteria can enter the blood via the renal vein, with resulting bacteraemia
Ureter
Infection here causes pyelonephritis
One-way urine flow
Organisms can ascend the ureters to the kidneys
Incompetence of cysto-ureteric valves can allow organisms to enter the upper urinary tract
Competent cysto-ureteric valves prevent reflux
Main access of organisms to lower urinary tract
Bladder
Regular micturition results in flushing out of bladder and urethra
Urethra

44 The renal tract. (a) Normal structure and physiology maintain a sterile tract. (b) Bacteria and yeasts can enter the renal tract by the urethra or blood.

temporarily related to coitus should be identified, so that prophylactic antibiotics can be recommended. If this is the case, the patient should also be advised to empty her bladder after coitus, helping flush out bacteria; good fluid intake aids this. Reinfection can be associated with use of the diaphragm with a spermicide, and an alternative method of contraception should be considered.

Uropathogenic strains of *Escherichia coli* that cause pyelonephritis in young women can also cause uncomplicated infections (usually cystitis) in young men.[9] Risk factors include anal intercourse, intercourse with a female partner with heavy introital colonization by a uropathogenic 'coliform', or lack of circumcision.[9]

There are important groups of patients where the symptoms of UTI may not be clear, and include the older patient with new or increased confusion, or a young child with a nonspecific febrile illness or irritability. Infants and children who have bacteriuria, with a fever of 38°C, or more should be considered to have acute pyelonephritis, as should those with fever of less than 38°C with loin pain/tenderness. In the UK, infants and children with bacteriuria but no fever or loin pain/tenderness can be regarded as having cystitis/lower urinary tract infection.[12] This guideline uses a 'traffic-light system' that enables the individual child to be identified as high-risk (red), intermediate-risk (amber), and low-risk (green) of serious illness as discussed in the UK NICE Guideline, *Feverish Illness in Children*.[13] All children under the age of 3 months, and all those over this age who are identified as being at high-risk of serious illness should be referred immediately to the specialist unit. Children who are classed as intermediate-risk should be considered for urgent referral as well; if not referred, they can, as with low-risk children, be managed in the community.[12, 13]

In general, only symptomatic patients should be tested for a UTI. This is especially important in the older patient (>65 years), where asymptomatic bacteriuria is common (>25% of women, and >10% of men).[14] Similarly screening for asymptomatic bacteriuria in young children is not recommended.[12]

However, asymptomatic bacteriuria in pregnancy can have serious risks for the mother (pyelonephritis and gram-negative septicaemia), and for the developing fetus (intrauterine growth retardation [IUGR]), as well as prematurity. Therefore, all pregnant women should be screened for asymptomatic bacteriuria in the first trimester and where this is identified it must be treated to reduce the risk.[15]

Asymptomatic bacteriuria in pregnancy is likely to occur in 2–7% of pregnancies, and of these, over 30% are estimated to develop pyelonephritis if untreated, placing the patient at an unacceptable risk of sepsis.[16] It is important to ensure that a clean-catch MSU is collected and the patient must be given clear instructions (preferably written) on how to do this. For asymptomatic bacteriuria to be confirmed, a pure growth of the same organism (>10^7 bacteria/L of urine) with same sensitivity pattern must be identified on at least two occasions. The second specimen is usually collected several days after the first, and if the same organism is grown, treatment with an appropriate antibiotic is given for 7 days. Some obstetric departments check for clearance 7 and 14 days after treatment is completed; local guidelines must be consulted. Patients who have asymptomatic bacteriuria should submit a MSU at each subsequent antenatal visit to check that bacteriuria has not recurred. Screening is also recommended before urological surgery, and in renal transplant patients.

PRIMARY CARE

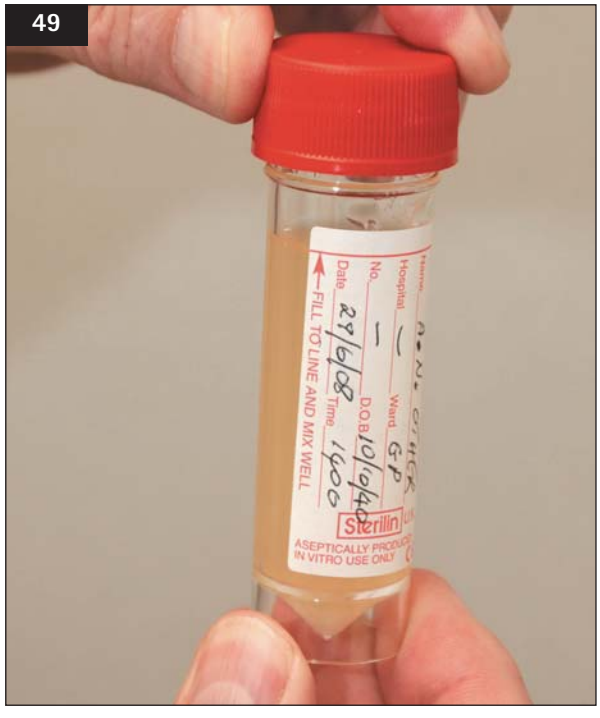
There should be suitable toilet facilities for patients to use to collect a specimen. Advice for the patient on collecting a MSU, and preferably an information sheet should be given. Suitable receptacles for collection should be available for the female patient in particular, as it is unreasonable to expect these patients to pass a clean-catch MSU into the laboratory specimen container; a supply of unused plastic cups is useful (these can be considered virtually 'sterile') (**45, 46**). If the patient is expected to collect the specimen at home the information should also detail other suitable collection containers. If the patient can use such an item safely, a dishwasher-cleaned glass jar can be used and following collection, the patient transfers urine to the laboratory specimen container.

45, 46 A supply of suitable receptacles should be available so that the patient can collect the MSU 'on site'. The standard specimen container is not suitable for women, and a supply of disposable plastic cups is useful (**45**). The practicality of using these in relation to the urine specimen container is clearly illustrated (**46**). Similar advice should be given when the patient collects the urine at home. For this purpose, these cups can be regarded as 'sterile'.

THE PATIENT

Reproducing in nutrient-rich urine, bacteria initiate an inflammatory response, and leukocytes enter the bladder in large numbers. Along with the inflammatory response, bacterial waste products, and compounds from dead and dying leukocytes, irritate the lining of the bladder and the urethra during micturition, giving rise to the classic symptoms of urgency, frequency, and dysuria. It is for relief of these symptoms that the patient seeks medical advice.

The patient should be reviewed with the Quick Action Guides, and the need to collect a specimen determined. For the young sexually active woman, with a 'first episode' of cystitis, the diagnosis can be straightforward, and empirical antibiotic treatment considered. Advice on bed rest as required, good fluid intake, and emptying the bladder completely before sleeping should be given. For all other patients who require investigation, an MSU should be collected and 'dipsticked' to determine further management, and the need to submit the specimen to the laboratory. Particular attention should be given to the child younger than 3 years, and national guidelines such as the UK NICE, Urinary Tract Infection in Children[12], and Feverish Illness in Children[13], referred to.



47–52 Urine collection. Written guidance should be given to the patient on how to collect the specimen. **(47)** The patient should ensure that their name, date of birth, and the date and time of collection are recorded on the specimen container before collection. **(48–50)** After collection, the urine should be carefully poured into the specimen container to the marked line, the lid *firmly* closed, and the container gently inverted 3–4 times to dissolve the boric acid crystals. **(51)** Excess urine should be poured into the toilet. **(52)** The used receptacle should be discarded safely. Hands should then be washed with soap and water.

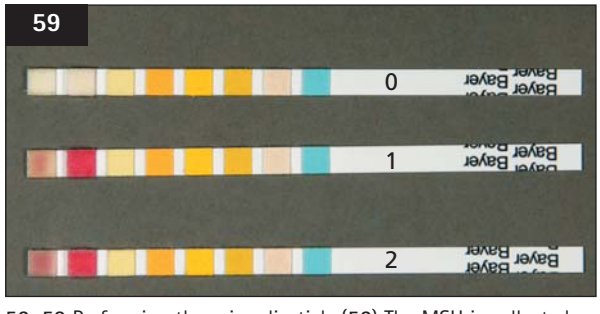
COLLECTING THE URINE SPECIMEN

Information on appropriate collection containers has been outlined (**45, 46**). A MSU should be collected, so that any contaminating bacteria in the urethra are flushed out first, and the sample represents the bladder contents. Collecting a specimen is relatively easy for men, provided the foreskin (if present) is fully withdrawn, the glans is clean, and a good stream is passed for several seconds before the MSU is collected in the container. Urine collection poses a problem for women, and instructions below should be given:

- Remove underwear completely.
- Sit on the toilet with the legs well apart.
- Hold the labia apart with the fingers of one hand.
- Use several 4 × 4 gauzes lightly soaked in soap from a pump action receptacle to clean the periurethral area from front to back in one motion.
- Do the same with water to ensure the area is then well rinsed; pat dry.
- Initiate the stream into the toilet for several seconds, and then collect the MSU in a suitable container (**45, 46**).
- Transfer the urine to the specimen container (**46**).

After collection, the patient pours the urine into the labelled specimen container up to the marked line, and the remainder of the sample is discarded. The lid should be firmly applied and the container inverted several times to ensure that boric acid crystals (where used) are dissolved (**47–52**). With young children, the process is more difficult and 'pads and syringes' can be used (**53–55**), although it is more practical for toddlers to pass urine into a potty.

53–55 Collection pads for obtaining urine specimens from young children, such as the Euron® Uricol Newcastle Urine Collector in the UK can be used. The child's genital area and bottom must be washed with soap (unmedicated) and water, well rinsed and dried. The pad is applied to the area where urine will be voided; for a baby the pad can be kept in place with a cotton disposable nappy fitted inside out (so that the nappy does not absorb urine). The pad should be checked every 10 minutes to see if it is wet. If there is no urine at 30 minutes, a fresh pad must be applied.
(53) The pad, collection tube, and syringe. **(54)** Drawing up the urine sample from the pad. **(55)** As a small volume of urine is usually obtained from a child, a white-topped container should be used. Boric acid containers should not be used in these circumstances, as the high concentration of boric acid in a smaller volume of urine will affect the viability of bacteria. If gloves are not available, hands should be washed with soap and water after the procedure. Such specimens must be transported promptly, and if there is a delay, placed in the refrigerator.



56–59 Performing the urine dipstick. (**56**) The MSU is collected into a suitable container. (**57**) The dipstick should be inserted into the urine specimen to ensure that all the panels are soaked, and then drained as it is pulled over the rim of the container. (**58**) The panels of the dipstick should be aligned with the correct panels on the dipstick container for reading. (**59**) It is important to read the manufacturer's instructions. Leukocyte esterase (first left panel) and nitrites (second left panel) are the relevant tests. These are read at 2 and 1 minutes respectively; the development of the leukocyte panel at 0, 1, and 2 minutes should be noted. Staff training and assessment should be in place. Although this is viewed as a simple procedure, without adequate training, including which tests are relevant to UTI, the test is often performed incorrectly.

The potty should be washed with hot water and washing-up liquid, well rinsed with hot water, and drained before collection of the urine. Cotton wool balls, gauze, or sanitary towels should not be used.

Examination of the specimen

When a urine specimen has been collected, it should be examined by eye; a crystal clear urine indicates that a UTI is unlikely. If there is any degree of 'cloudiness', the specimen should be dipsticked for nitrite and leukocyte esterase, using the manufacturer's instructions (**56–59**). It is essential to use a MSU. Dipstick testing has been employed in a number of settings, which emphasizes that staff training is necessary to perform and interpret the result.[17, 18] Positive nitrite and leukocyte esterase tests show the presence of bacteria and inflammatory cells in the urine, and confirm cystitis. For the majority of sexually active women with their 'first episode' of cystitis, a dipstick result can be used to confirm the clinical diagnosis, and empirical antibiotic treatment considered; there is no need to send the specimen to the laboratory (see Quick Action Guide).

For children 3 years and older, dipsticks testing for nitrite and leukocyte esterase is diagnostically as useful as microscopy, and can be used.[12] However, there is a risk of missing a proportion of cases of acute UTI in infants and children younger than 3 years; frequent bladder emptying flushes out bacteria, and the nitrites they produce. Reduced retention times in the bladder thus leads to a lower nitrite level, which may not be recorded on the dipstick. Contaminated urine is common with noninvasive sample collection from infants and children who are not toilet trained. A summary of key points (from the UK NICE Guidelines [2007]) referring to the criteria for specimen collection and examination which determine the need to send a specimen to the laboratory is shown in **60** and **61**.[12] The use of urgent microscopy of urine specimens to guide treatment decisions, and the overall practicality of such a service has been discussed.[19]

60 An algorithm for use in primary care that can be used in managing a child 3 months or older, but <3 years with a suspected UTI *who does not require immediate referral to the paediatrician*, and can be managed in primary care.* (Adapted and reproduced from NICE *CG 54 Urinary Tract Infection: Diagnosis, Treatment, and Long-Term Management of Urinary Tract Infection in Children*, www.nice.org.uk/CG54.[12] With permission of NICE.)

60

Symptoms and signs to consider in the child 3 months or older but <3 years with a suspected UTI:

Fever, abdominal pain, loin tenderness, urine frequency or dysuria, vomiting, poor feeding, lethargy, irritability, haematuria, offensive urine, failure to thrive.[12]

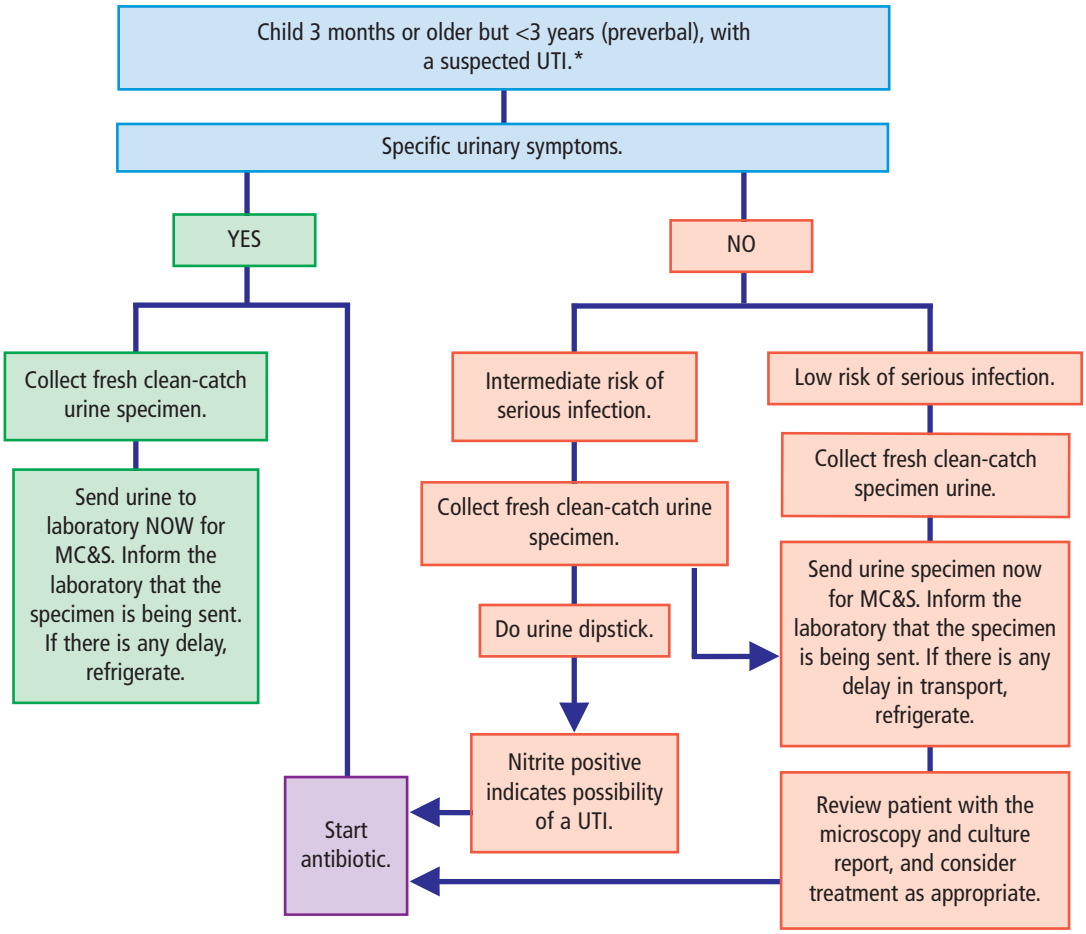
Any child with an unexplained fever of 38°C or more must have a urine tested within 24 hours.[12]

Local guidelines for assessment and referral of children to specialist care should be in place, based on NICE Clinical Guideline 54 and Feverish Illness in Children (NICE Clinical Guideline 47).[12, 13] The traffic light system is used to assess the severity of illness (high, intermediate, or low) to make the decision to refer or manage in primary care. If there is a high risk of serious illness, or the child is less than 3 months of age, refer urgently to the local paediatric unit.*

General indications for sending a urine specimen for culture:[12]

- Acute pyelonephritis/upper urinary tract infection
- A high to intermediate risk of serious illness
- Younger than 3 years
- A single positive result for leukocyte esterase or nitrite
- Recurrent UTI
- An infection that does not respond to treatment in 24–48 hours
- When clinical symptoms and dipstick tests do not correlate

Symptomatic infants and children with a positive urine culture should be treated.[12]


Child 3 months or older but <3 years (preverbal), with a suspected UTI.*
Specific urinary symptoms.
YES
NO
Collect fresh clean-catch urine specimen.
Send urine to laboratory NOW for MC&S. Inform the laboratory that the specimen is being sent. If there is any delay, refrigerate.
Intermediate risk of serious infection.
Collect fresh clean-catch urine specimen.
Do urine dipstick.
Nitrite positive indicates possibility of a UTI.
Start antibiotic.
Low risk of serious infection.
Collect fresh clean-catch specimen urine.
Send urine specimen now for MC&S. Inform the laboratory that the specimen is being sent. If there is any delay in transport, refrigerate.
Review patient with the microscopy and culture report, and consider treatment as appropriate.

61

Symptoms and signs to consider in the child 3 years or older with a suspected UTI:

Dysuria, frequency, dysfunctional voiding, changes in continence, abdominal pain, loin tenderness, fever, vomiting, haematuria, offensive urine, cloudy urine, malaise.

Any child with an unexplained fever of 38°C or more must have a urine tested within 24 hours.[12]

Local guidelines for assessment and referral of children to specialist care should be in place, based on NICE Clinical Guideline 54 and Feverish Illness in Children (NICE Clinical Guideline 47).[12, 13] The traffic light system is used to assess the severity of illness (high, intermediate, or low) to make the decision to refer or manage in primary care. If there is a high risk of serious illness (or the child is less than 3 months of age) refer urgently to the local paediatric unit.*

General indications for sending a urine specimen for culture.[12]

- Acute pyelonephritis/upper urinary tract infection.
- A high to intermediate risk of serious illness.
- Younger than 3 years.
- A single positive result for leukocyte esterase or nitrite.
- Recurrent UTI.
- An infection that does not respond to treatment in 24–48 hours.
- When clinical symptoms and dipstick tests do not correlate.

Symptomatic infants and children with a positive urine culture should be treated.[12]

Child 3 years and older (verbal), with a suspected UTI.*

↓

Collect clean-catch urine (MSU) specimen.

↓

Do dipstick for leucocytes and nitrites.

↓

Leukocyte esterase POSITIVE, nitrite POSITIVE: The child should be regarded as having a UTI, and antibiotic treatment should be started. (If the child has a high or intermediate risk of serious illness and/or a past history of UTI, a urine sample should be sent for MC&S).

Leukocyte esterase negative/nitrite POSITIVE: Antibiotic treatment should be started. Send urine for MC&S.

Leukocyte esterase POSITIVE/nitrite negative: Send urine for MC&S. Only start treatment if there is good clinical evidence of UTI. Leukocyte esterase may be indicative of infection outside the urinary tract, and the need for different management (e.g. vaginitis, balanitis). Review with microscopy and culture result.

Leukocyte esterase and nitrite are negative: UTI unlikely, and there is no need to send a urine to the laboratory, unless there are specific indications, such as recurrent UTI. Treatment for a UTI should not be started and other causes of the illness should be investigated.

The urine specimen is being sent to the laboratory:

- Inform the laboratory now.
- If there is a delay in transport, refrigerate in designated practice refrigerator.

61 An algorithm for use in primary care that can be used in managing a child >3 years of age with a suspected UTI *who does not require immediate referral to the paediatrician.** (Adapted and reproduced from NICE *CG 54 Urinary Tract Infection: Diagnosis, Treatment, and Long-Term Management of Urinary Tract Infection in Children*, www.nice.org.uk/CG54.[12] With permission of NICE.)

In primary care, urgent microscopy would usually not be feasible, and the algorithms in **60** and **61** are a reasonable basis to establish protocols in primary care, in conjunction with the paediatricians and the microbiology laboratory. As specimens from children will often be of smaller volume, they are likely to be collected into a specimen container without boric acid, and must be stored in the designated refrigerator if there is any delay in transport.

THE REQUEST FORM

In addition to the clinical details, recent, current, or proposed antibiotics, as well as antibiotics allergies can be included on the form.

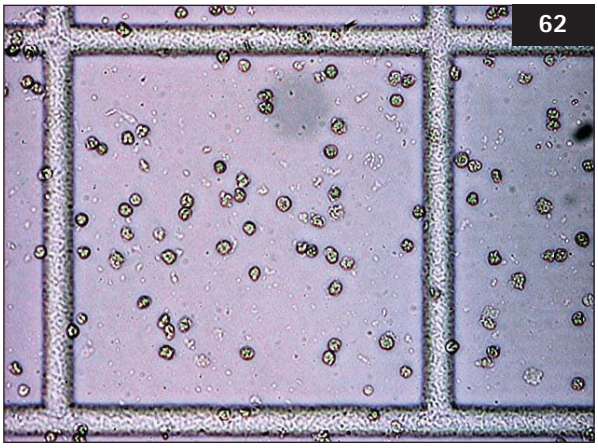
THE LABORATORY REPORT

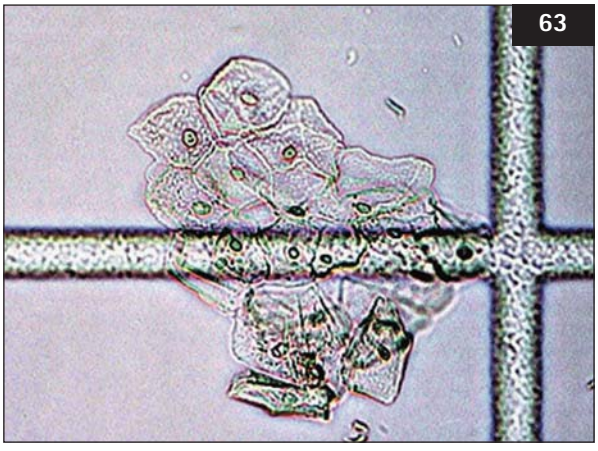
As the urine report will be the most common result that needs interpretation, it is important to review all the information recorded.

Laboratories usually do microscopy on urine specimens, when white blood cells (WBC), red blood cells (RBC), and epithelial cells numbers are quantified (**62, 63**). Increasingly, automated microscopy particle counting machines are being used, which detect the presence of particles (bacteria) and WBC at and above a set limit. Essentially, parameters can be selected and set, for example, at 1×10^6 particles (bacteria)/L (that is below 10^7 bacteria/L, the number considered 'significant' in a UTI), and a white cell count (WCC) of 10×10^6/L (the minimum number of WBC that indicate inflammation).[1] Specimens that meet one or both of these criteria will be 'selected' by the automated microscopy machine for culture. If neither of these criteria are met, only the microscopy result is issued, with the comment 'No microscopical evidence of a UTI'. All other specimens will be cultured and antibiotic susceptibility tests done on relevant isolates. For certain groups of patients, such as children, renal transplant patients, and haematology/oncology patients, laboratories will process all specimens for culture irrespective of an automated microscopy result.

White cell count

The presence of WBC in the urine (pyuria) is used as a marker of inflammation, usually (but not exclusively) indicating infection. With UTI, WCC are frequently in excess of 100×10^6/L, and the local laboratory may set a minimum cut-off with its users, so for example, a count of 10×10^6/L or more can be considered as 'significant'.[1] Note that WBC in a urine specimen may originate from anywhere in the urinary tract (urethra, bladder, kidney). They may also contaminate the specimen coming from either the vagina, or a balanitis.





62, 63 Light microscopy of an MSU showing (**62**) numerous WBCs and (smaller) bacterial particles. (**63**) The clump of epithelial cells shows a poorly taken specimen (note absence of white cells), where urine turbulence has washed these vaginal epithelial cells into the specimen. Bacteria of the vaginal flora will also be cultured and can convert a 'true UTI' into a mixed growth or turn an insignificant growth into a mixed growth or even a pure significant growth of a contaminant!

WBC are usually recorded on reports in a range of:

Number of WBC/mL: 0–100 (or >100 × 10^3/mL)

or

Number of WBC/L: 0–100 (or >100 × 10^6/L)

Red blood cell count

Red blood cells are not a useful marker of a UTI. Their presence can be an indication of other pathologies. RBC are usually recorded on reports in a range of:

Number of RBC/mL: 0–100 (or >100 × 10^3/mL)

or

Number of RBC/L: 0–100 (or >100 × 10^6/L)

For clinical purposes, when automated microscopy machines are used, the level below which RBC are not considered significant should be agreed with the local urology team. Reports should state for example that 'The presence of 25 × 10^6/L RBC or less, is not regarded as significant in renal pathologies'. This value may be higher than is accepted for standard urine microscopy, but it should be noted that automated machines also detect empty 'ghost' RBC.

Epithelial cells

The presence of epithelial cells recorded by microscopy essentially applies to females, and indicates contamination of the specimen with vaginal cells; the specimen is thus not a clean-catch MSU. Adherent to these cells will be resident members of the vaginal flora. If the specimen is stored incorrectly, or there is a delay in transport and processing, this flora can reproduce, thereby converting what might have been reported as a pure or predominant growth into a 'profuse mixed growth'. Epithelial cells are usually reported as follows:

Epithelial cells: Not seen
Epithelial cells: Scanty
or Moderate
or Profuse

The relative number of epithelial cells must be used to interpret the relevance of the culture report.

The bacterial count

Most women with acute onset cystitis will have more than 10^8 bacteria/L, and this is regarded as a 'significant bacteriuria'.[9] However, up to a half of women with cystitis are considered to have a lower bacterial count in their urine, and the term 'acute urethral syndrome' has been used to refer to this entity.[20] It has been proposed that counts of between 10^5 and 10^8/L may represent the early stage of cystitis.[21] In addition, sexually transmitted infections, such as chlamydia and gonococcus, should be considered in the sexually active woman with urethritis, and an insignificant titre of a uropathogen[9] (see Chapter 4).

A summary of the criteria used to interpret a urine report is shown in **64**. Because of the issues associated with specimen collection, the microbiology of urine cannot be an exact science, so while the 'gold standard' highlighted in **64** is the optimum result, it is essential to review the report with the clinical presentation of the patient, and if antibiotics were given, the susceptibility profile of reported bacteria. If there is one or more of the criteria in **64** below the grey line, this points towards the specimen being less representative of a UTI. In this regard, the laboratory should include helpful comments to aid interpretation.

When detected by microscopy, organisms such as yeasts, trichomonas and threadworm (*Enterobius vermicularis*) are reported; occasionally spermatozoa may be seen. These are usually introduced by contamination of the urine specimen with vaginal secretions at the time of collection.

Antibiotics

Laboratories should report an appropriate number of antibiotics on the report, preferably with at least two agents that the organism is susceptible to, to take into account allergy to β-lactam antibiotics in particular. However, more resistant organisms such as the ESBL-'coliforms' may limit the oral antibiotics available to a single agent such as nitrofurantoin or ciprofloxacin. Where there are limited treatment options in the setting of a confirmed UTI, especially that which is not responding to empirical treatment, then the medical microbiologist should be contacted.

64

Practical ranges of the four parameters are shown below. If there is one or more of the four parameters below the grey line, the specimen is less likely to represent a UTI. The combination of parameters must be interpreted with the clinical presentation.

WBC x 10^6/L	Epithelial cells seen	Bacterial (colony) count /L	Growth description
>100	None	$>10^8$	Pure growth of...
10–100	None	$>10^7$ to $<10^8$	Predominant growth of...
<10	Scanty	$>10^6$ to $<10^7$	Mixed growth of...
0	Moderate/profuse	$>10^6$	No significant growth
			NO GROWTH

64 Four parameters are used in the interpretation of the urine microscopy and culture report in the symptomatic patient. For each parameter, the 'gold standards' are:

- There is pyuria (preferably >100 × 10^6 WBC/L).
- There are no epithelial cells present (i.e. the specimen is clean-catch MSU).
- There is a significant growth of bacteria, usually $>10^8$ colonies/L.
- There is a pure growth of one organism; a UTI is essentially caused by a single bacterial species.
- (Increased fluid intake with frequent micturition can reduce bacterial counts to 10^7–10^8 colonies/L.)

STERILE PYURIA

The reasons for 'No growth' in a urine should be reviewed with the possible causes of sterile pyuria (**65**).[22] Fever in children can also result in pyuria.[23] There may be straightforward reasons, such as recent antibiotic use, or in the male patient a urethritis due to a STI. With ongoing symptoms, it is worthwhile to consider infection with fastidious organisms, and the medical microbiologist should be contacted so that special culture conditions can be used in an attempt to culture such pathogens.

TREATMENT

Antibiotics

Empirical treatment guidelines are given in Chapter 11. In general, a 3-day course of the antibiotic is suitable for treating infections such as cystitis in otherwise healthy females, as longer courses show no benefit in outcome (see Chapter 2). For UTI in pregnancy and in men, a 7-day course is recommended. Either the laboratory report, or the return of the patient with treatment failure, can lead to modification of therapy. Reports may not include susceptibility information to cefalexin or ciprofloxacin, whose use is discouraged because of the risk of CDAD. If there are specific instances where use of these agents may be considered, the medical microbiologist can be contacted for information and advice. As discussed previously, a quinolone such as ciprofloxacin is usually the only oral option available to treat pseudomonas.

Children 3 months or older with an upper UTI should be treated for 7–10 days with either co-amoxiclav or cefalexin. For a lower UTI, 3 days of amoxicillin (if the organism is sensitive), trimethoprim, nitrofurantoin, or cefalexin can be used.[12] Local guidelines must be consulted.

If a child with a likely UTI has not responded to treatment after 24 hours, the parents/carer should return with the child for reassessment. The laboratory should be contacted to find out the progress on the specimen. If antibiotic susceptibility results are available, these can be used to guide treatment.

Prophylactic antibiotics

Where there are more than two episodes of infection/year associated with coitus, post-coital trimethoprim, co-trimoxazole (USA), cefalexin, or nitrofurantoin can be offered[9] (see Chapter 11). Prompt post-coital micturition, with good fluid intake may prevent initiation of infection.

65

Treatment/noninfective causes
- Recent antibiotic therapy
- Recent surgery
- Analgesic nephropathy
- Foreign bodies in the genitourinary tract, including catheters
- Tumours of the genitourinary tract

STD
- Male patients in particular
- Obtain detailed history and do full examination of genitalia
- For males send a 'first catch' specimen for gonococcal and chlamydia PCR

Vaginal discharge
- Pus cells from vaginal contamination; review previous examination. Has an HVS been done?

Tuberculosis
- An early morning urine (EMU) should be sent to exclude this infection in the renal tract

Other possible causes
- Fever in children
- Uncommon infection with fastidious organism such as haemophilus or rarely anaerobes
- Uncommon infection with fastidious organism such as mycoplasma; consider empirical clarithromycin if other options excluded
- Patient on recent trimethoprim or co-trimoxazole. Consider nutritionally deficient, thymidine-dependent 'coliforms'

65 Possible causes of a sterile pyuria.

Cranberry juice

Cranberries contain a number of organic substances including catechin, flavinoids, and organic acids; these compounds may prevent adhesion of bacteria to the bladder wall, and hippuric acid has an antiseptic effect.[24] Limited evidence suggests that cranberry products can help to prevent recurrence of UTI in women at risk of developing these infections. The optimum regimes for this have not been established. There is no evidence to support the use of cranberry products in treating current UTI, but as it consistently acidifies urine, it could prevent the growth of aerobic bacteria such as *Pseudomonas aeruginosa*, and may be considered.

SUMMARY AND KEY POINTS

While recognizing that asymptomatic bacteriuria is a common finding in the older patient (>65 years) for which intervention is not required, it is important to collect a MSU in the symptomatic patient. When a resistant organism such as an ESBL-producing *Escherichia coli* is identified, for example in the symptomatic patient, prompt advice should be sought if there is no suitable oral option. Where OPAT is not available, the patient needs referral to hospital. It is important that the referral letter clearly alerts the emergency department physician about the 'ESBL status' of the patient, so that the correct antibiotic(s) can be given immediately after collection of blood cultures and a MSU, and infection control alerted so that the patient is nursed in a side-room from the outset.

It is worthwhile now to review the Quick Action Guides, and the information discussed at the end of Chapter 2. This stated that women with UTI have indicated that they do want to avoid taking antibiotics, and thus the unwanted side-effects associated with their use.[25] For each patient there should be a full review of their symptoms, thereby assessing the need to collect a specimen. A cost-effective approach to managing uncomplicated UTI in women in the community could involve immediate antibiotic prescription based on dipstick testing, or empirical delayed prescription, with the patient fully understanding the management decision.[26] Delayed prescription can reassure patients, and validate their experience of their own symptoms, and their reason for visiting the primary care physician on each occasion.[26] When assessing each patient with a likely UTI, the last step in the whole process should be the informed decision to send the specimen to the laboratory.

In summary the following points should be noted:

- The practice/clinic should establish guidelines for clinical and nursing staff to use so that there are set criteria, centred on the Quick Action Guides and critical steps of **40**.
- These should be used regularly as a training tool to give guidance on when and how to collect specimens from the various patient age groups, storage and transport of specimens, and how the laboratory report should be interpreted.
- Additional guidelines are required for the management of UTI in children in the community. The information in **60** and **61** can be used as the basis for this guidance. Critical steps 1, 2, and 4 of **40**, and **53–55** should be referred to.
- Recognition of the entity of asymptomatic bacteriuria in the older patient is crucial. Unnecessary specimens generate laboratory reports that result in inappropriate antibiotic prescription, which can give rise to serious complications.

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4 The Genital Specimen

- Introduction
- Organisms and epidemiology
- Specific issues associated with the genital specimen
- Primary care
- The patient
- Collecting the specimen
- The request form
- The laboratory report
- Treatment
- Summary and key points

INTRODUCTION

The scenario given in **66** is an example of where the laboratory report was seen as a directive to give antibiotic treatment, which would have resulted in unnecessary antibiotic prescription. This introduces a number of important principles relating to the genital specimen. As with other specimens in this book, the critical steps begin with deciding whether to test, collecting the correct specimen through to interpretation of the result.

Genital tract specimens in particular are of note for the following reasons:

- There is a wide range of organisms that grow in the genital tract, and they need to be recognized as members of the normal flora, and/or as potential pathogens, or true pathogens.
- The requirement to sample specific sites in order to obtain the highest chances of detecting certain organisms.
- Recognizing when a patient is likely to have a sexually transmitted infection (STI) and refer to the sexually transmitted diseases (STD) clinic.
- Recognizing the inherent problems of diagnosing certain STI in primary care due to the labile nature of certain organisms.
- In relation to STI in particular, knowing the alternative diagnostic methods that are available for use in primary care if the patient is unable to attend the STD clinic. This is particularly important for the labile gonococcus.
- Being aware that there are a number of simple bed-side tests that can be done in primary care to diagnose the most common causes of a vaginal discharge. This permits immediate management of the patient and minimizes wasting resources.
- The management of the 'worried well'.

The aim of this chapter is to highlight the issues in primary care relevant to the genital tract specimen. The Quick Action Guides summarize the main points in assessing the patient, collecting the specimen, and giving treatment.[1,2] Of key importance is considering the possibility of the patient having a STI, including 'blood-borne' viruses such as human immunodeficiency virus (HIV), and advising the HIV test.[3]

66 The HVS specimen. An example of the consequences of acting on a report of a specimen which is collected outside the primary care setting, and there is an inappropriate instruction to give treatment. The steps in the process can be divided into seven critical steps (see Chapter 1, 1).

In this scenario, at critical step 1, the collection of a HVS on the post-natal ward was reasonable. The laboratory reports the presence of group B streptococcus. At critical step 7, this result is reviewed on the post-natal ward, and is communicated to the patient's primary care practice/clinic with instructions to prescribe treatment. As the patient is penicillin-allergic, the primary care physician telephones the laboratory and speaks to the microbiologist asking which antibiotic can be given. It is then confirmed that the patient is well; there is no need to give an antibiotic. While group B streptococcus can cause infection in operation wounds in obstetrics and gynaecology, it is a member of the normal vaginal flora, and does not cause a vaginal discharge in the otherwise healthy woman. If there had been an appropriate antibiotic to use on the report, it is likely that the patient would have been given this, irrespective of the fact that treatment was not necessary.

Storing and transport of the standard bacteriology genital specimen swab

Buffered semi-solid charcoal 'transport swabs' are used. The environment in these 'transport swabs'[4] is such that it can maintain the viability of both aerobes and anaerobes for several days, without allowing their multiplication. The swab should be well loaded with as much of the appropriate sample as possible. If there is a delay in transport to the laboratory, the specimen should be refrigerated; viable organisms can be recovered for up to 72 hours. In order to maximize the recovery of labile bacteria such as *Neisseria gonorrhoeae*, it is best that swabs are transported to the laboratory and 'plated out' on the day of collection.

66

CRITICAL STEP 1:
Is collection of a specimen indicated?

A patient who is about to be discharged from the post-natal ward 2 days after a normal vaginal delivery, complains of a 'bit of spotting'. Examination is unremarkable, but a HVS is collected before discharge.

The breast-fed baby is well.

CRITICAL STEP 2:
Obtain a good quality specimen.

A HVS swab is taken appropriately, using a transport swab.

CRITICAL STEP 3:

Record the full patient and clinical details and type of specimen on the request form. Where necessary, record the specific test request.

Request form states: '? PV bleed'.

CRITICAL STEP 4:

How is the specimen stored and what is the frequency of transport to the laboratory?

CRITICAL STEP 5:

What is the quality of the laboratory process, including turnaround times?

CRITICAL STEP 6:

Is immediate or routine reporting of this result required by the laboratory?

CRITICAL STEP 7:
How is the laboratory report interpreted?

Report on AB 34 years, female:
PV bleed 2 days after NVD.

Culture report:
Profuse growth of group B streptococcus:

Penicillin:	S
Erythromycin	R
Tetracycline	R

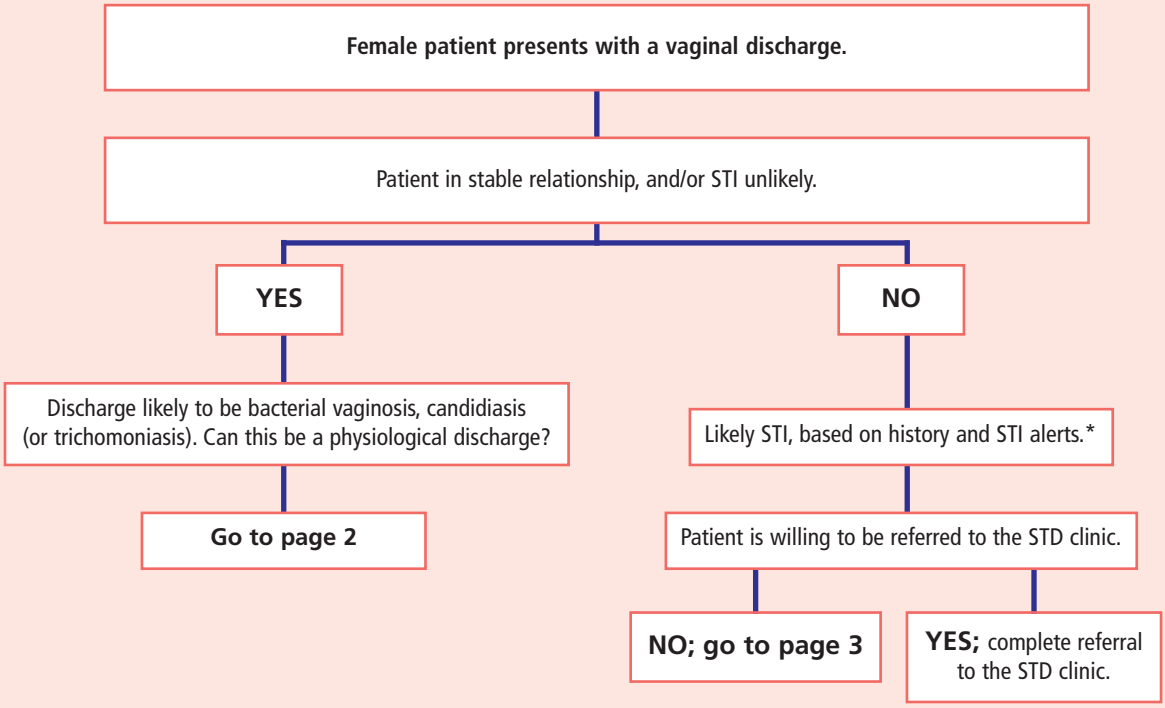
On reviewing the report 2 days later, the midwife on the post-natal ward phones the practice/clinic nurse and tells her that the patient requires treatment for the group B streptococcus.

The primary care physician phones the microbiologist to ask which antibiotic can be given, as the patient is allergic to penicillin.

The microbiologist states that if the patient is well, and there is no evidence of infection, treatment for the streptococcus is not warranted. The primary care physician confirms that the patient and baby are well.

Quick Action Guide – Female – 1

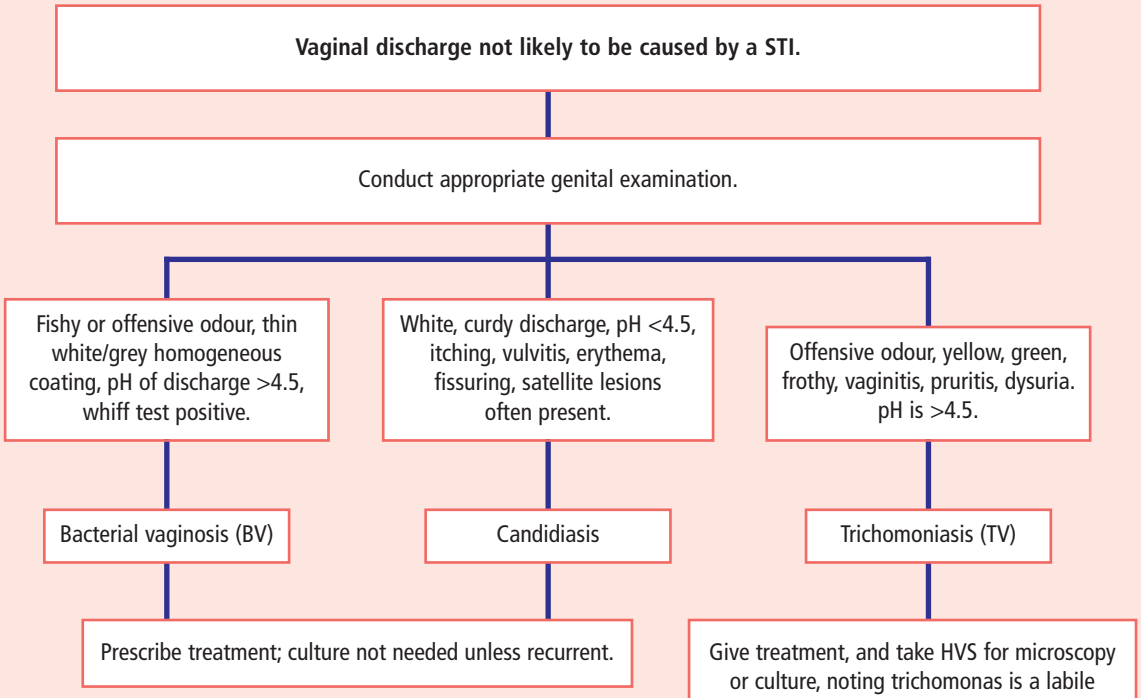
(Adapted from information in *Management of Abnormal Vaginal Discharge in Women; Quick Reference Guide for Primary Care* and *Diagnosis of Chlamydia; Quick Reference Guide for Primary Care*.[1, 2] With permission of the UK Health Protection Agency.


Female patient presents with a vaginal discharge.
Patient in stable relationship, and/or STI unlikely.
YES
NO
Discharge likely to be bacterial vaginosis, candidiasis (or trichomoniasis). Can this be a physiological discharge?
Likely STI, based on history and STI alerts.*
Go to page 2
Patient is willing to be referred to the STD clinic.
NO; go to page 3
YES; complete referral to the STD clinic.

*STI alerts for the female patient:

- 13–25 years of age.
- Previous history of STI, partner with STI, multiple partners.
- Unprotected sex, nature of sexual practice.
- Menstrual abnormalities: post-coital/intermenstrual bleeding.
- Deep dyspareunia.
- Suspected PID (pelvic pain and tenderness).
- Frequency/dysuria with culture negative MSU.
- Reactive arthritis.
- Conjunctivitis.

Quick Action Guide – Female – 2



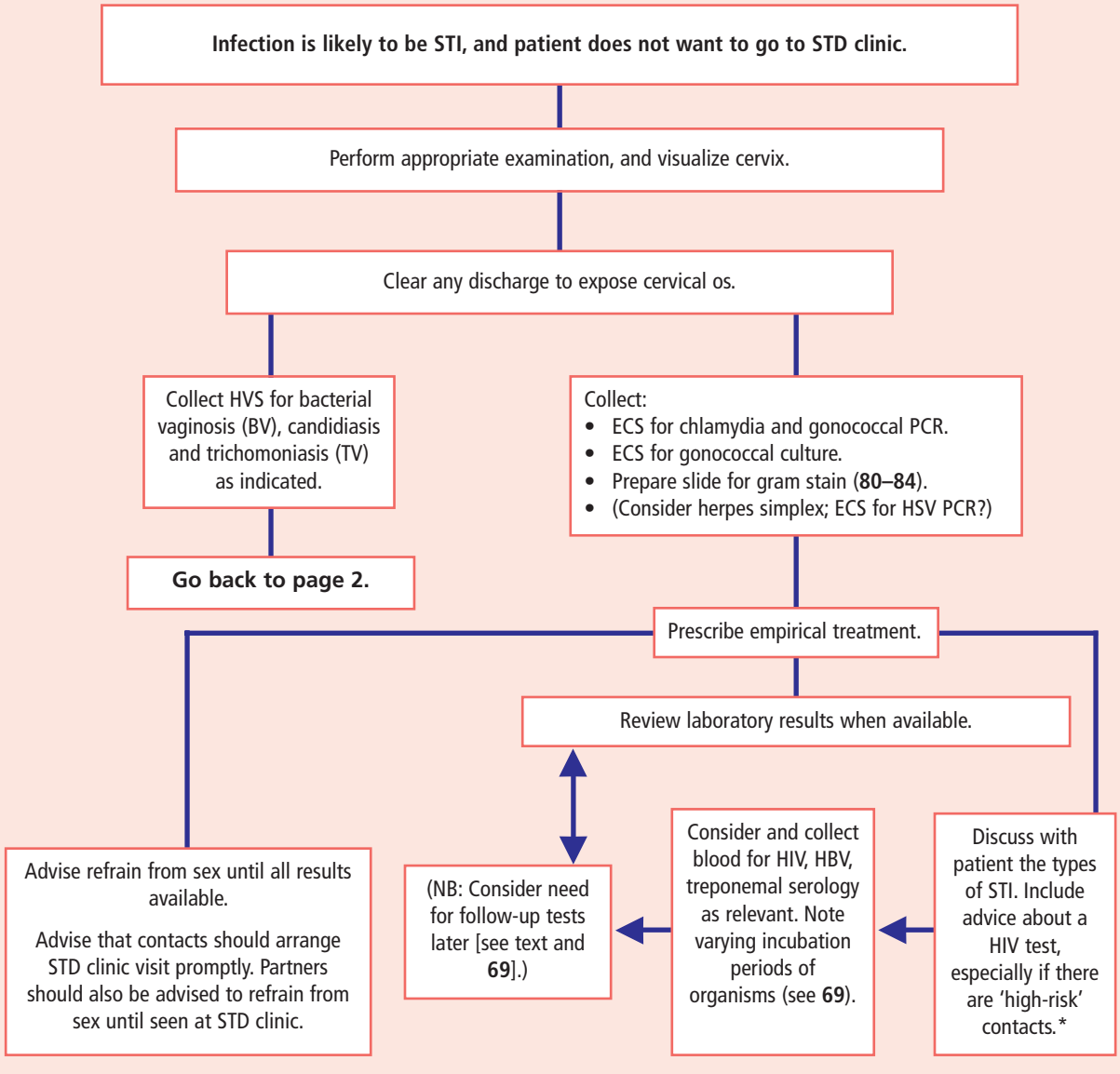
Always send an HVS when:

- The diagnosis is unclear.
- Postnatal.
- Pre and post termination of pregnancy.
- Pre and post gynaecology surgery.
- Recurrent episodes (>3/year).
- Symptoms not characteristic of BV or candidiasis.
- Vaginitis without discharge.

DO AN ECS FOR CHLAMYDIA AND GONOCOCCAL PCR, IF POSSIBLE STI OR PID

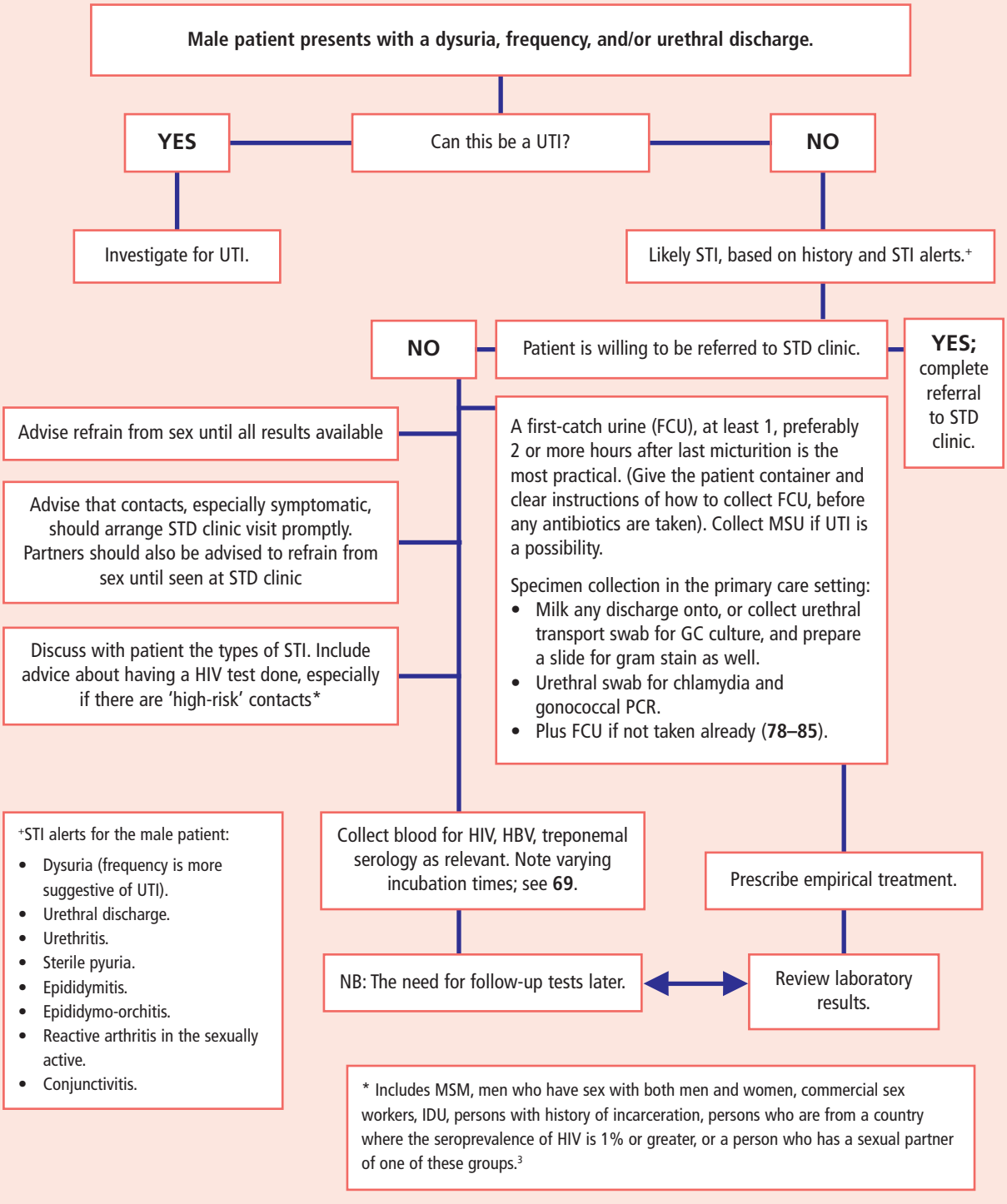
Discuss chlamydia screening with the sexually active patient. If chlamydia is identified, it does not necessarily mean infidelity in this relationship, as it can be a chronic, often asymptomatic infection.

Quick Action Guide – Female – 3

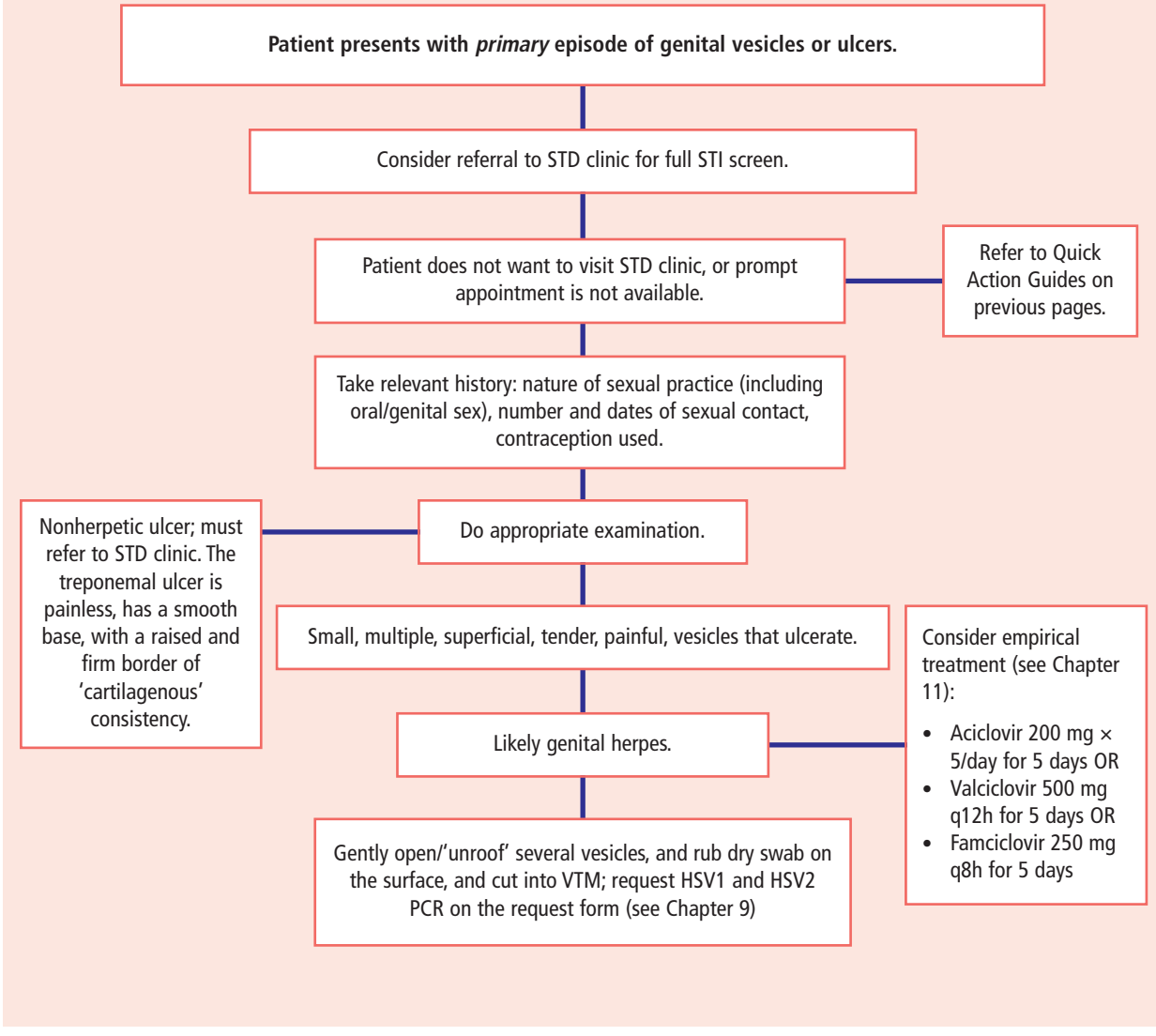

Infection is likely to be STI, and patient does not want to go to STD clinic.
Perform appropriate examination, and visualize cervix.
Clear any discharge to expose cervical os.
Collect HVS for bacterial vaginosis (BV), candidiasis and trichomoniasis (TV) as indicated.
Go back to page 2.
Collect:
• ECS for chlamydia and gonococcal PCR.
• ECS for gonococcal culture.
• Prepare slide for gram stain (80–84).
• (Consider herpes simplex; ECS for HSV PCR?)
Prescribe empirical treatment.
Review laboratory results when available.
Advise refrain from sex until all results available.
Advise that contacts should arrange STD clinic visit promptly. Partners should also be advised to refrain from sex until seen at STD clinic.
(NB: Consider need for follow-up tests later [see text and 69].)
Consider and collect blood for HIV, HBV, treponemal serology as relevant. Note varying incubation periods of organisms (see 69).
Discuss with patient the types of STI. Include advice about a HIV test, especially if there are 'high-risk' contacts.*

* Includes MSM, men who have sex with both men and women, commercial sex workers, IDU, persons with history of incarceration, persons who are from a country where the seroprevalence of HIV is 1% or greater, or a person who has a sexual partner of one of these groups.[3]

Quick Action Guide – Male


Male patient presents with a dysuria, frequency, and/or urethral discharge.
Can this be a UTI?
YES
NO
Investigate for UTI.
Likely STI, based on history and STI alerts.+
Patient is willing to be referred to STD clinic.
NO
YES; complete referral to STD clinic.
Advise refrain from sex until all results available
Advise that contacts, especially symptomatic, should arrange STD clinic visit promptly. Partners should also be advised to refrain from sex until seen at STD clinic
Discuss with patient the types of STI. Include advice about having a HIV test done, especially if there are 'high-risk' contacts*
A first-catch urine (FCU), at least 1, preferably 2 or more hours after last micturition is the most practical. (Give the patient container and clear instructions of how to collect FCU, before any antibiotics are taken). Collect MSU if UTI is a possibility.
Specimen collection in the primary care setting:
• Milk any discharge onto, or collect urethral transport swab for GC culture, and prepare a slide for gram stain as well.
• Urethral swab for chlamydia and gonococcal PCR.
• Plus FCU if not taken already (78–85).
+STI alerts for the male patient:
• Dysuria (frequency is more suggestive of UTI).
• Urethral discharge.
• Urethritis.
• Sterile pyuria.
• Epididymitis.
• Epididymo-orchitis.
• Reactive arthritis in the sexually active.
• Conjunctivitis.
Collect blood for HIV, HBV, treponemal serology as relevant. Note varying incubation times; see 69.
Prescribe empirical treatment.
NB: The need for follow-up tests later.
Review laboratory results.
* Includes MSM, men who have sex with both men and women, commercial sex workers, IDU, persons with history of incarceration, persons who are from a country where the seroprevalence of HIV is 1% or greater, or a person who has a sexual partner of one of these groups.3

Quick Action Guide


Patient presents with *primary* episode of genital vesicles or ulcers.
Consider referral to STD clinic for full STI screen.
Patient does not want to visit STD clinic, or prompt appointment is not available.
Refer to Quick Action Guides on previous pages.
Take relevant history: nature of sexual practice (including oral/genital sex), number and dates of sexual contact, contraception used.
Nonherpetic ulcer; must refer to STD clinic. The treponemal ulcer is painless, has a smooth base, with a raised and firm border of 'cartilagenous' consistency.
Do appropriate examination.
Small, multiple, superficial, tender, painful, vesicles that ulcerate.
Consider empirical treatment (see Chapter 11):
• Aciclovir 200 mg × 5/day for 5 days OR
• Valciclovir 500 mg q12h for 5 days OR
• Famciclovir 250 mg q8h for 5 days
Likely genital herpes.
Gently open/'unroof' several vesicles, and rub dry swab on the surface, and cut into VTM; request HSV1 and HSV2 PCR on the request form (see Chapter 9)

ORGANISMS AND EPIDEMIOLOGY

A list of organisms associated with the genital tract, either as members of the 'normal flora', or as pathogens/potential pathogens, is shown in **67**. Some of these organisms and the conditions they are associated with are given in more detail in the Appendix.

The microbiology of the female genital tract is very complex, having a rich 'normal flora', which includes small numbers of potential pathogens such as candida and *Gardnerella vaginalis*. In the vagina, the microbial population is not only influenced by the menstrual cycle, but also by the age of the individual. Group B streptococcus is frequently reported on high vaginal swab (HVS) specimens, and of all the organisms is the one most likely to cause confusion when a report is reviewed. Not infrequently swabs are submitted to the laboratory with clinical details such as 'Previous group B streptococcus; still present after treatment', inferring numerous repeat courses of antibiotics.

67 A list of organisms associated with the genital tract. These are either organisms that can be cultured, or identified by other means such as NAAT, or those that are identified by serological tests, such as HBV and HIV. See appendix, chapter 4 for more detailed information.

67

Usually considered to be part of the normal vaginal flora

Lactobacilli
Group B streptococcus*
Staphylococcus aureus (both MSSA and MRSA)*
Anaerobes*
*Gardnerella vaginalis** (in low numbers as part of the normal flora)
Candida spp. (in low numbers as part of the normal flora)
('Coliforms')*
(*Pseudomonas aeruginosa*)*

* Can be important in post-surgical infections, post-partum infections, malignancies of the genital tract

Vaginal discharge

Bacterial vaginosis	*Gardnerella vaginalis* *Mobiluncus* spp. (anaerobes)
Candidiasis	*Candida albicans* and other *Candida* species
Trichomoniasis	*Trichomonas vaginalis*

Vulvovaginitis, including pre-pubertal girls

Group A streptococcus
Haemophilus influenzae
Streptococcus pneumoniae
Enterobius vermicularis
Neisseria gonorrhoeae in pre-pubertal girls

Sexually transmitted infections (STI)

Acute pelvic inflammatory disease	*Neisseria gonorrhoeae* *Chlamydia trachomatis* (plus gardnerella, anaerobes, streptococci)
Cervicitis	*Neisseria gonorrhoeae* *Chlamydia trachomatis* HSV2
Conjunctivitis (adult)	*Neisseria gonorrhoeae* *Chlamydia trachomatis*
Conjunctivitis (ophthalmia neonatorum)	*Neisseria gonorrhoeae* *Chlamydia trachomatis*
Genital ulcers	HSV1 and HSV2 *Treponema pallidum* *Haemophilus ducreyi*
Pharyngitis (asymptomatic)	*Neisseria gonorrhoeae*
Proctitis	*Neisseria gonorrhoeae* *Chlamydia trachomatis*
Syphilis	*Treponema pallidum*
Trichomoniasis	*Trichomonas vaginalis*
Urethritis – gonococcal	*Neisseria gonorrhoeae*
– non-gonococcal	*Chlamydia trachomatis*

Viruses

– Hepatitis A virus	HAV (anogenital-oral sex)
– Hepatitis B virus	HBV
– Human immundeficiency virus	HIV
– Cervical carcinoma	HPV 16, 18
– Genital warts (condylomata acuminata)	HPV 6, 11

Pelvic inflammatory disease

Acute
Chlamydia trachomatis
Neisseria gonorrhoeae
Chronic
Chlamydia trachomatis, Gardnerella vaginalis, mixed 'coliforms', mixed anaerobes, (actinomyces)

Actinomycosis

Actinomycosis associated with IUCD use	*Actinomyces israelii*

Essentially, this organism is relevant in neonatal sepsis, when it is acquired by the neonate from the maternal vaginal flora at the time of delivery, and it can cause wound infections in obstetrics (retained products, episiotomy wound abscess) or gynaecological surgery. Apart from these situations, group B streptococcus is considered a commensal organism. It does not elicit an inflammatory response in the vagina and is not a cause of uncomplicated vaginal discharge.[5] However, it is often the only organism reported on a genital swab sent to the laboratory for microscopy, culture, and sensitivity (MC&S), which leads to it being given undue prominence. One might ask why medical microbiology laboratories report the presence of group B streptococcus. The main reason is that it can give rise to problems cited above. Request forms often lack clinical details about pregnancy or recent surgery, so the organism is reported as a caution, in case the information is needed at, for example, the time of delivery.

When group B streptococcus is identified in a HVS taken during pregnancy, this finding must be noted in the patient's file, as an alert to give antibiotic prophylaxis when there are complications at the time of birth, such as maternal fever, pre-term labour, and prolonged rupture of membranes.[5] There is no role for giving antibiotics in an attempt to eradicate group B streptococcus during pregnancy.

The presence of methicillin-sensitive *Staphylococcus aureus* (MSSA) or methicillin-resistant *Staphylococcus aureus* (MRSA) in a vaginal specimen of an otherwise healthy woman represents vaginal/perineal flora, and is unlikely to be significant, although the association of toxic shock syndrome with tampon use is recognized but uncommon.[6] Either of these bacteria, as well as 'coliforms' and anaerobes, as members of the 'normal flora' can cause abscesses in an obstetric or gynaecological surgery wound.

Group A streptococcus, unlike group B streptococcus, is not a member of the normal vaginal flora. In the past it was the major cause of puerperal sepsis, with significant morbidity and mortality. Group A streptococcus and two other 'respiratory tract' bacteria, *Streptococcus pneumoniae* and *Haemophilus influenzae*, should be regarded as pathogens and treated whenever identified in the genital tract. Group A streptococcus is not an infrequent cause of vulvo-vaginitis in pre-pubertal girls, causing perianal cellulitis or vaginal discharge.[7] *Enterobius vermicularis* may cause vaginal irritation and should be considered in young girls, and women, with persistent symptoms when no other cause has been identified.

Genital tract specimens, mainly HVS, are the next commonest bacteriology specimen type sent to the laboratory after urines. Examining several hundred consecutive specimens from the genital tract shows that female patients account for over 98% of all swabs received (**68**). Of these, over 60% are from individuals in the ages of 20–49 years. The majority of swabs are collected from young women presenting with vaginal discharge and/or soreness who often assume they have 'thrush'. Older women may complain of soreness, with bacterial or atrophic vaginitis.

Conspicuous by their absence in the data in **68** are specimens from young sexually active men, who would usually self-refer to the STD clinic. In young men a urethral discharge will usually be due to a STI. Of the few males included in the data in **68**, the swabs were mainly taken in the setting of balanitis.

SPECIFIC ISSUES ASSOCIATED WITH THE GENITAL SPECIMEN

STI are a particular challenge in primary care, and are best managed at STD clinics, where there is direct access to laboratory facilities, including microscopy for trichomonas and gonococcus, direct culture for gonococcus, as well as counselling and contact tracing in a confidential environment.

STI are a complex group of infections, involving a wide range of organisms each with specific diagnostic and treatment challenges. A comprehensive account of their management in primary care is given by Lazaro.[8] STI are often asymptomatic, and the individual may have more than one STI. The complexity of STI is compounded by changing social behaviour. A study by the UK Health Protection Agency in 2008 showed a marked increase in the number of individuals over the age of 45 years presenting to STD clinics with STI, the majority of which were genital warts and herpes. This study pointed out that older people are less likely to consistently use condoms (because the risk of pregnancy is reduced), which along with increased international travel, internet dating, drugs to counter erectile dysfunction, and overlapping sexual networks are all factors that contribute to the increase in sexual activity.[9] Individuals of all ages may be at risk, and this includes HIV infection. A case report in the *New England Journal of Medicine* discusses a patient who was diagnosed with HIV infection at the age 81; here oral/oesophageal candidiasis was the presenting illness.[10] This case emphasizes that HIV needs to be considered in a sexually active adult of any age.

PRIMARY CARE

Good communication between the microbiology department, primary care, and the STD clinic are important, to ensure that the best testing protocols are adopted in keeping with national guidance, such as the use of nucleic acid amplification tests (NAAT). *Neisseria gonorrhoeae* is a labile organism meaning that it will often not be viable (and hence not isolated) when swabs are sent to the laboratory. This is one reason why STD clinics have a small laboratory so that samples are directly plated onto the appropriate media, and incubated at 37°C in a CO_2 atmosphere before being transported to the laboratory. Reproducing such facilities in primary care is much more difficult or impossible, and NAAT, which detects nonviable organisms, may be the only way of making a reliable diagnosis. 'Dual' testing NAAT kits detect both chlamydia and gonococcus in the same swab, and are now the recommended test.[11,12] This methodology is not a panacea, as sensitivity testing is not possible without a live organism.

'Bed-side' tests

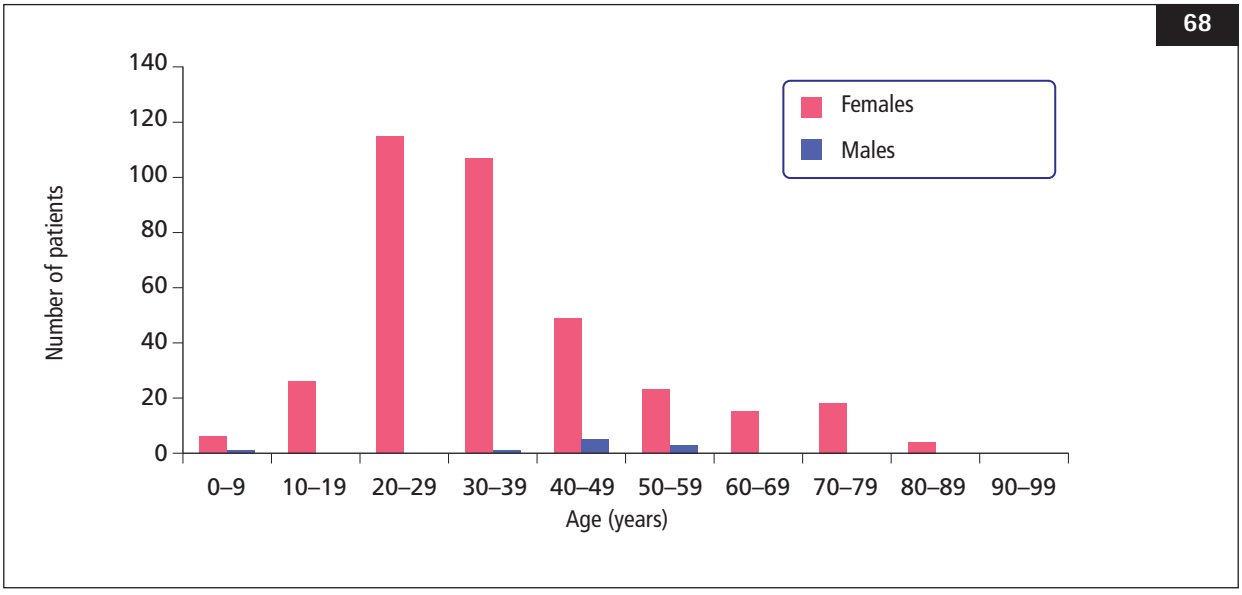
There should be facilities for simple tests such as 'pH paper' and the 'whiff' test for diagnosing bacterial vaginosis.[13] It is also feasible to consider the addition of a microscope, where with suitable training 'wet preps' to diagnose candida and trichomonas could be done in primary care. Other reasonable 'on-site' testing can be considered in discussion with the local medical microbiology department. If the transport service is co-ordinated with a community sexual health service in primary care, agar plates can be inoculated for culture of gonococcus, and placed in sealed 'sandwich' boxes in a CO_2 enriched atmosphere using 'gas-packs'. There is no loss of viability of gonococcus here in a period of less than 5 hours at room temperature.[12] This would be reasonable for developing an enhanced sexual health service in primary care in conjunction with the local STD clinic and microbiology laboratory.

THE PATIENT

This section discusses the sexually active patient, which as highlighted above, can cover a span of ages,[9,10] The Quick Action Guides should be used.

The worried well patient

Both male and female patients can be 'worried well', and consider that they have had a recent 'unplanned' sexual contact, and are seeking an 'all clear' before resuming an ongoing relationship. This is in contrast to the situation where there is the immediate need for post-exposure prophylaxis[3] (see Chapter 9). If there is any doubt about managing the situation, the patient must be referred promptly to the STD clinic. When giving advice to the 'worried well', an understanding of the incubation period of the various organisms is required, which in turn determines when the first and subsequent



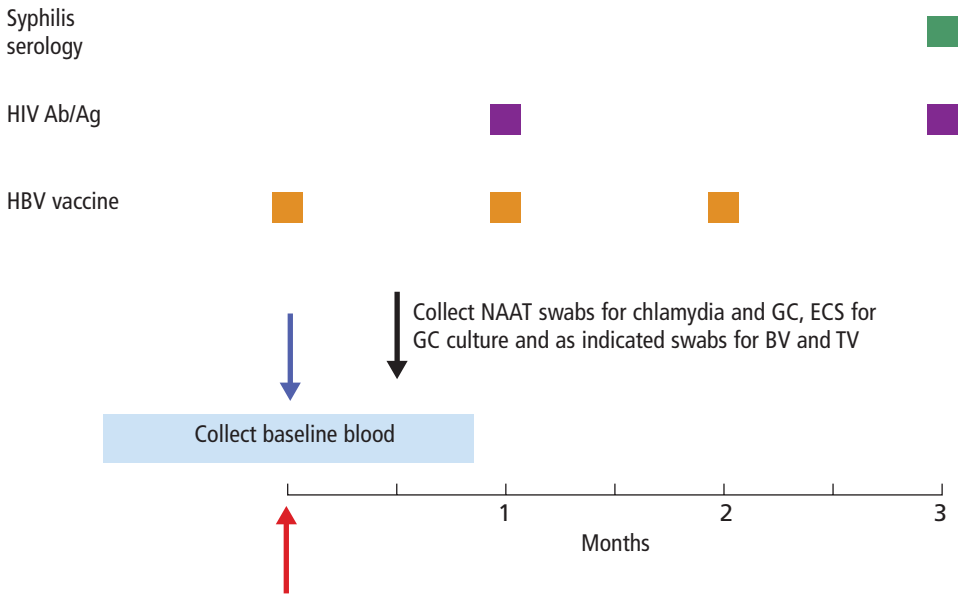
68 The typical age and sex distribution of patients submitting genital swab specimens to the laboratory over a 1 week period.

tests should be done for each organism in order to give the 'all clear'. Figure **69** highlights key time points to consider with various organisms. This information can be used to develop a local policy with the STD clinic that determines which patients need immediate referral to the clinic for assessment of an exposure, and those who can be safely defined as 'worried well'. Testing for HIV at 1 month (4 weeks) will detect the great majority of individuals who have been infected, provided the laboratory uses the appropriate test. A negative result at 1 month is very reassuring/highly likely to exclude HIV infection. An additional test should be offered to everyone at 3 months (12 weeks) to definitely exclude HIV infection.[14]

The sexually active female, and her partner, may be concerned about an ongoing discharge where no diagnosis has been made, resulting in self- or physician-driven prescription of repeat courses of antibacterial and antifungal treatment.[15] Not infrequently these are normal vaginal secretions, which may be copious on occasion, are odourless, do not itch or irritate, or stain underwear, and have a pH of 3.5–4.6. In these circumstances, the patient and her partner should be reassured.

69

Such cases should be referred to the STD clinic. If testing is done in primary care, and based on locally agreed protocols, the information here should be the basis for the tests.
In this example, the red arrow = incident and blue arrow = primary care appointment the next day.
The information given here can be the basis of a locally agreed policy in primary care.



Points to consider following a potential exposure are listed below, and take into account the incubation period of different organisms, which directs the timing of the first, and subsequent test time, for example HIV.[3, 14]

- A baseline blood can be collected for serum storage in the local microbiology laboratory. These samples are stored for up to 2 years, and can be referred to if a positive serology result is found on subsequent blood samples.
- In the asymptomatic 'worried well', and where no antibiotics have been given, they should be screened at 2 weeks for chlamydia, gonococcus, and as indicated for BV and TV. The timing here takes into account the minimum incubation period of chlamydia of 5 days.
- A rapid course of HBV vaccine can be started.
- HIV Ab/Ag test. The first test is done at 4 weeks, and later where clinically indicated.
- Treponemal serology can be done at 12 weeks.

69 General factors to consider for a 'worried well' patient asking for an 'all clear' following an 'unplanned' sexual exposure.

The patient with a simple discharge

This includes bacterial vaginosis (BV) and, candidiasis; where with certain 'bed-side tests' the diagnosis can be made, and treatment prescribed.[1] This not only gives the patient an immediate result but can save the health-care economy money. Trichomoniasis would also be considered, but its relevance to STI means that gonococcus and chlamydia would also need to be considered.

The patient is likely to have a STI

If the patient is likely to have a STI, referral to the STD clinic is the preferred option. However, if the patient does not want to go to the clinic, the appropriate Quick Action Guide should be used, in order that the essential tests are done. Infections of the genital tract can have a significant impact on social relationships, and correct advice should be given. For example, the finding of chlamydia in one partner of a stable relationship does not necessarily mean infidelity in this relationship, as chlamydia can be a long-term asymptomatic infection acquired some time ago. When managing the patient who may potentially have a STI, the information in 70 is a reminder of the key points to consider.

70

High-risk contacts are considered in these groups: MSM, men who have sex with both men and women, commercial sex workers, IUCD, persons with history of incarceration, persons who are from a country where the seroprevalence of HIV is 1% or greater, or a person who has a sexual partner of one of these groups[3]

(a) Sexually active females (especially <25 years)

- Menstrual abnormalities: post-coital/intermenstrual bleeding
- Mucopurulent cervical discharge
- Inflamed/friable cervix (which may bleed on contact)
- Deep dysparunia
- Urethral syndrome: frequency/dysuria with culture negative MSU
- Suspected PID (pelvic pain and tenderness)
- Reactive arthritis
- Conjunctivitis

(b) Sexually active males of any age

- Dysuria (frequency is more suggestive of UTI)
- Urethral discharge
- Urethritis
- Sterile pyuria
- Epididymitis, epididymo-orchitis
- Reactive arthritis
- Conjunctivitis

(c) Individuals in these groups should be screened for asymptomatic chlamydia infection

- Sexually active men and women <25 years with a new sexual partner in the last 12 months
- Women <25 years having their first cervical smear
- Sexual partners of those with proven or suspected chlamydia infection
- Women undergoing cervical instrumentation (IUCD)
- Parents of infants with chlamydial conjunctivitis or pneumonitis
- All patients with another STI, including genital warts
- (All women seeking termination of pregnancy)
- (Semen and egg donors)
- (Tubal infertility or ectopic pregnancy)

70 Criteria to consider in 'high-risk' contacts, as well as the testing alerts for chlamydia in symptomatic **(a)** females and **(b)** males.[2] **(c)** Screening for asymptomatic infection should be done in individuals in these groups; those groups in brackets would be under the care of the obstetrician or gynaecologist.

COLLECTING THE SPECIMEN

When a genital specimen is taken to confirm the diagnosis of candida, BV, or trichomonas, a well loaded HVS is collected using a transport swab (see Quick Action Guide). Specific clinical features of these infections, together with use of specific tests such as the 'whiff' test can be useful in making the diagnosis, thereby reducing the need to submit a swab (**71, 75**).

A summary of tests to use in the diagnosis of STI in female and male patients is shown in **72**, with photographic illustrations of the various aspects of specimen collection given in **73–85** on pages 82, 83. A detailed account of NAAT testing is given by Johnson *et al.*[12]

STI – the female patient

The cervix should be visualized, and an endocervical swab (ECS) for gonococcal culture collected first. It is relatively simple to use a swab to make a smear on a microscope slide, which is air dried, and sent to the laboratory (in a safety container) for a gram stain (**80–84**, page 83). The NAAT swab is then inserted 1–2 cm into the endocervical canal, i.e. past the squamo-columnar junction, and rotated against the wall of the endocervix at least twice, or for the period of time recommended by the manufacturer. The swab should then be withdrawn without touching the walls of the vagina, and placed in the appropriate container of the kit.

Urethral specimens should be obtained as directed by the manufacturer. Specimens should be collected at least 1 hour after the patient last voided urine. A specimen for culture can be collected first. The NAAT swab for chlamydia and gonococcus should then be inserted 1–2 cm into the urethra, and rotated at least once in one direction.

When investigating symptomatic women for chlamydia, a first-catch urine (FCU) is not the optimum specimen, as the sensitivity of the test varies but is lower than an ECS and a self-taken vulvo-vaginal swab (VVS).[16] (A self-taken VVS is the preferred tests for population screening as in this situation one is willing to sacrifice some loss of sensitivity for the practicality of not having to take an ECS, which is time consuming and demanding on resources). If a FCU is taken, this should be directed by the manufacturer. Where practical, and the patient has booked an appointment through the primary care physician for the next day, it is reasonable for her to obtain the container from the practice/clinic (and that for a mid-stream urine [MSU] as necessary), and collect the FCU (and MSU) after overnight sleep. There will be maximum 'capture' of organisms in the FCU. If this cannot be done, the FCU should be collected at least 1 hour, and preferably 2 hours or more after the patient last voided urine. Urine specimens are not suitable for culture of gonococcus.

71

Condition	Symptoms and signs	pH*	Wet mount (microscopy)	Comment
Bacterial vaginosis (BV)	Thin light grey homogeneous discharge, fishy odour (Whiff test positive**)	>4.5	Clue cells***	Replacement of normal flora, and thus greatly decreased lactobacillus population and increased population of curved gram-negative rods****
Candidiasis	Pruritis, dysuria and burning, vaginal erythema, thick, curdy discharge	<4.5	Hyphae/spores***	Mixed infection with BV and/or TV can occur
Trichomoniasis (TV)	Pruritis, dysuria, yellow, frothy discharge, increased odour	>4.5	Motile protozoa	Symptoms increase with higher pH

*Normal pH is <4.0; litmus pH paper should be used to determine the pH of the discharge
Addition of a few drops of 10% KOH to a smear of the discharge on a glass slide releases a strong 'fishy' odour (75**).
***With a small investment in a microscope and training these two conditions could be readily diagnosed in the primary care Practice
****Culture is very sensitive, and small numbers of *Gardnerella vaginalis* do not correlate with clinical infection

71 Characteristic features of bacterial vaginosis, candidiasis and trichomoniasis in a vaginal discharge.

72

Organism	Female		Male	
	Symptomatic	**Asymptomatic**	**Symptomatic**	**Asymptomatic**
Chlamydia	ECS	ECS as part of STI screen Self taken vulvo-vaginal for population screening	FCU* Urethral swab**	FCU*
Chlamydia-conjunctivitis	Remove pus with sterile gauze, evert lower eyelid and rub the swab on the palpebral conjunctiva		Remove pus with sterile gauze, evert lower eyelid and rub the swab on the conjunctiva	
Gonococcus	ECS	ECS done as STI screen	Urethral swab** FCU	Not done
Herpes virus	Open ulcer, rub swab on ulcer base, and cut into VTM*** for PCR (Chapter 9, **150–153**)	Not done	Open ulcer, rub swab on ulcer base, and cut into VTM*** for PCR (Chapter 9, **150–153**)	Not done
Treponema	Dark field microscopy in STD clinic		Dark field microscopy in STD clinic	
	Serology	Serology	Serology	Serology
Trichomonas****	Wet mount in STD clinic Acridine orange stain Culture	Not done	Wet mount in STD clinic Acridine orange stain Culture	Not usually done

*First catch urine (FCU) in the early morning is preferable; urine held for at least 1–2 hours is usually submitted.

**Usually taken after the FCU is collected.

****Local laboratory protocol should be used.* Here a supply of 'in date' viral transport medium (VTM) needs to be available. After rubbing the swab in the ulcer base, the swab is placed in the VTM, and cut off, and the lid firmly applied. As an alternative the dry swab cut into a sterile container can be submitted (see Chapter 9). Send for HSV PCR.

****Trichomonas is a labile organism, and microscopy should be done promptly if wet mounts are done. The sensitivity of wet mount is 50–90%, acridine orange stain 66%, and culture 85–90%. The availability of tests such as culture should be discussed with the local medical microbiology department.

72 Tests done for chlamydia, gonococcus, HSV, syphilis, and trichomonas.

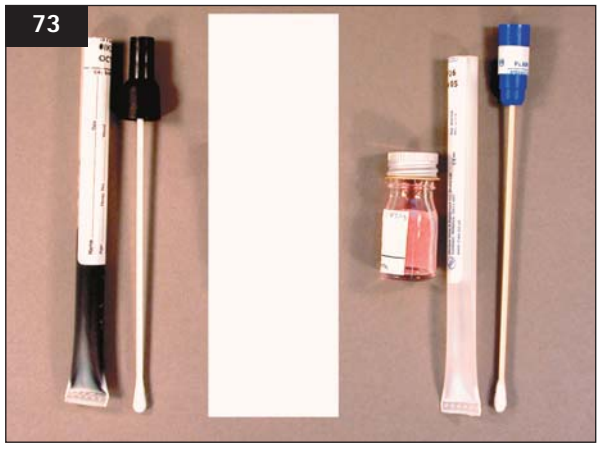
STI – the male patient

For the male patient who does not want to visit the STD clinic, a FCU is the most practical test. If the patient has booked an appointment through the primary care physician for the next day, it is reasonable for him to obtain the container from the practice/clinic (and that for an MSU as necessary), and collect the FCU (and MSU) after overnight sleep. There will be maximum 'capture' of organisms in the FCU. If this cannot be done, the FCU should be collected at least 1 hour and preferably 2 hours or more after the patient last voided urine. Urine specimens are not suitable for culture of gonococcus.

Urethral specimens should be obtained as directed by the manufacturer. Specimens should be collected at least 1 hour after the patient last voided urine. A urethral swab for culture should be collected first. It is relatively simple to use a swab to make a smear on a microscope slide, which is labelled and air-dried, and sent to the laboratory (in a safety container) for a gram stain (**80–84**). The NAAT swab should then be inserted 2–4 cm into the urethra, and rotated at least once in one direction, or as directed by the manufacturer.

THE REQUEST FORM

The request form must state the relevant clinical details, for example pregnancy, post-partum, post surgery. Individual laboratories may not do all tests on every specimen, and local guidelines should be used. It may be necessary to stipulate specific tests on the request form such as BV or trichomoniasis (*Trichomonas vaginalis* [TV]) on the request form.



73–77 Examples of specimen collection for infections of the genital tract in the female. Local advice of the STD clinic and medical microbiology departments should be sought concerning the tests available in primary care. (**73**) Left: a transport swab can be used to collect a HVS to investigate bacterial vaginosis or candidiasis. Right: After a herpetic vesicle has been gently opened, the base is rubbed with a swab which is then cut in viral transport medium (VTM) for herpes PCR (see Chapter 9, **150–153**). (**74**) When collecting an endocervical swab for chlamydia and gonococcal PCR, the large swab should be used to remove discharge from the cervical os. The smaller diameter swab from the PCR kit is then inserted into the endocervix, and rotated several times to collect cellular material. This swab is placed into the PCR transport tube, 'snapped-off' (**78, 79**), and the cap firmly applied so that it embraces the top of the swab. (**75**) Using a sterile plastic loop, a sample of a vaginal discharge can be collected, and placed on a glass slide. Addition of 1–2 drops of 10% KOH, and the production of a 'fishy odour' confirms bacterial vaginosis. (**76**) For information only: This self-taken 'dry' swab is used, for example in national screening programmes for chlamydia, using NAAT. The swab is inserted several centimetres into the vagina and gently rotated. (**77**) When a IUCD loop is removed, and sent to the laboratory (actinomyces; see Appendix), it should be placed in a sterile white-topped container.

78–85 (**78**) An example of a swab for chlamydia and gonococcal PCR in the male. The swab is advanced several centimetres into the urethra, and rotated several times to collect the sample. (**79**) The swab is then 'snapped-off' in the transport tube, and the cap applied firmly to embrace the top of the swab. This picture shows the 'snap' site. (**80, 81**) If facilities are available for microscopy and culture, a sterile plastic loop can be inserted into the meatus and advanced several centimetres. The loop is then rotated to collect material. (**82**) The loop can be used to inoculate selective agar for culture. Providing the appropriate facilities are available for holding plates in a CO_2 atmosphere, and there is prompt transport to the laboratory, this is a useful way of maximizing the culturing of gonococcus in primary care. (**83**) The loop can be used to make a smear on a glass microscope slide, air dried, and sent in a safe transport container to the laboratory for examination. (**84**) A gram stain of a urethral discharge of a male with urethritis; the presence of gram-negative diplococci in a male patient essentially confirms the presence of *Neisseria gonorrhoeae*. (**85**) A first-catch urine should preferably be collected 'first thing' in the morning, and at least 1 hour, preferably 2–4 hours after the last micturition.

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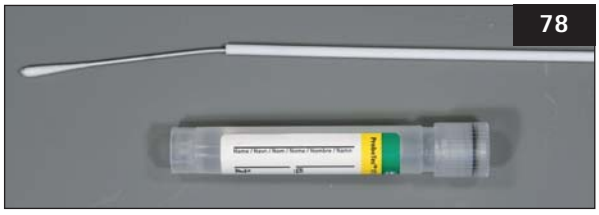

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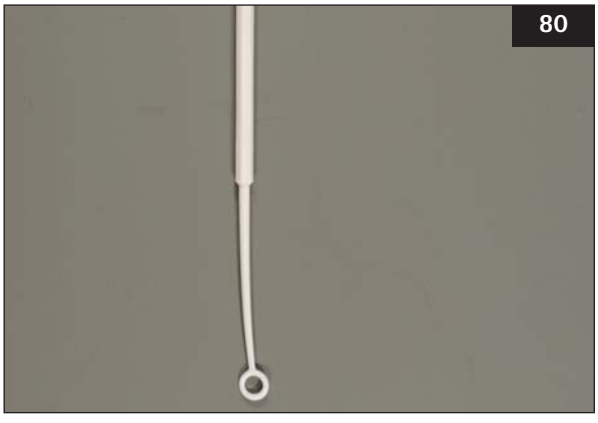

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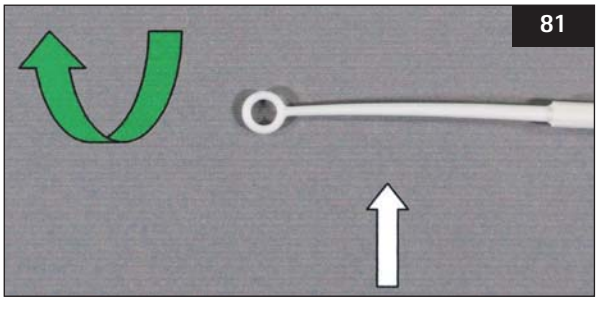

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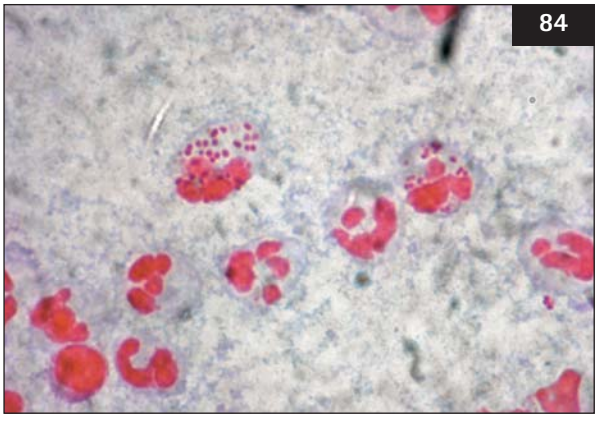

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THE LABORATORY REPORT

The laboratory report on the genital specimen will state the particular organism(s), and as relevant the antibiotic susceptibility profile. It is important to ensure all the details are reviewed, and the relevance of a particular organism noted. The report can state 'No pathogens isolated. Please note the presence of group B streptococcus'. As stated previously, group B streptococcus would not require treatment in an otherwise healthy woman with a discharge, whereas group A, C, and G streptococci would. Note that a scanty growth of candida may only represent its presence in the normal vaginal flora and does not indicate that the patient has thrush. The results of other tests, such as HIV serology, should be reviewed.

TREATMENT

Treatment of common genital infections is given in Chapter 11. For gonococcus, local guidelines used by the STD physicians should be consulted, as these will take into account a number of factors, including local changes in susceptibility profiles. In the USA, resistance to ciprofloxacin in gonococcal isolates rose from 0.2% in 1990 to 14% in 2006, resulting in specific guidance on when to avoid quinolones.[16]

In the case of STI, patients should be advised to abstain from sexual intercourse until the patient and partner have completed 7 days of treatment, or 7 days after a single dose of azithromycin. (Note that the 1 g dose of azithromycin may not effect cure of gonococcus.)

Where patients are compliant with treatment, and there is no risk of reinfection from a partner, test of cure is not needed. Because less effective agents such as erythromycin may be used in the treatment of chlamydia in pregnancy, test of cure should be done 5–6 weeks after treatment. The reason for this delay is that the sensitive molecular tests will detect dead organisms for several weeks, potentially giving a false-positive result.

SUMMARY AND KEY POINTS

A summary of key points with the genital tract specimen is given below. These are:

- The practice/clinic should establish guidelines for clinical and nursing staff to use so that there are set criteria, centred on the Quick Action Guides and the critical steps of **66**.
- Appreciation that the microbiology of the genital tract is extremely complex, and that there is a rich 'normal flora', that includes bacteria that have the potential to cause infection.
- Appreciation that group B streptococcus is a common member of the normal vaginal flora in the otherwise healthy woman, and its finding in these circumstances does not warrant antibiotic treatment. (It is relevant in the setting of 'at risk' labour/neonatal sepsis and post partum/surgical wound infection).
- Recognition that group A streptococcus, haemophilus, and pneumococcus are abnormal findings in the genital tract, in females of any age, but are more common in pre-pubertal girls and treatment should be given (gonococcal vaginitis can also occur in pre-pubertal girls).
- To differentiate UTI from STI in the sexually active male with urethritis.
- Recognition that gonococcus and trichomonas are labile organisms and their viability will be quickly lost in conventional swabs during transport to the laboratory. NAAT testing is the alternative for gonococcus.
- These should be used regularly as a training tool to give guidance on when and how to collect specimens from the various patient age groups, storage and transport of specimens, and how the laboratory report should be interpreted.
- Recognition of the key features in relation to STI:
  - Many STI are asymptomatic.
  - If there is one STI in an individual, there are likely to be others.
  - Recognition that the FCU specimen is not the ideal test for diagnosing chlamydia infection in the sexually active female, as up to 1/5 cases may be missed.
  - Compliance with treatment can be a problem.
  - Tracing of contacts, and treating them as well is essential.
  - Comprehensive advice must be given to reduce the risk of STIs.
  - Advising the patient to have an HIV test.

In relation to the sensitivity of NAAT tests, one manufacturer of Chlamydia NAAT has shown with reference to culture that for females, the sensitivity of an ECS is about 93%, while that of a FCU is about 80% (specificity over 98%). For males the sensitivity of a urethral swab (US) and FCU was similar at about 94% (specificity for US 94% and FCU 91%). VVS, currently used for national screening programs for chlamydia in certain countries, have a similar sensitivity to cervical testing for chlamydia.[17]

5

The Swab of the Chronic Leg Ulcer

- Introduction
- Organisms and epidemiology
- Specific issues associated with the chronic leg ulcer swab
- Primary care
- The patient
- Collecting the specimen
- The request form
- The laboratory report
- Treatment
- Summary and key points

INTRODUCTION

This chapter is primarily concerned with the 'wound swab' collected from the chronic leg ulcer. **The key points here are:**

1. Knowing when to swab an ulcer.
2. How to swab an ulcer.
3. Interpreting the laboratory report.

Figure **86** highlight these points, and with the Quick Action Guides can be used as a training tool to highlight the critical steps in the collection of a swab from an ulcer.[1] The principles that are discussed here apply to taking a swab from post-surgical wounds.

ORGANISMS AND EPIDEMIOLOGY

A list of the common bacteria that are associated with ulcers is shown in **87** (page 90). A wide range of organisms can be grown from ulcers, many of which are unlikely to cause infection. However, even the isolation of a well-recognized pathogen such as *Staphylococcus aureus* from a wound does not mean it is causing infection. An organism can either colonize a wound surface, being resident there, or causing infection, to which the body mounts an inflammatory response. Distinction between the two requires a clinical assessment of the wound/ulcer to determine if there is evidence of infection. Hence critical step 1 in the Introduction is key to management; staff must be trained to know when it is appropriate to take a specimen. Inappropriate collection of samples should not be accepted; this is a quality issue because it is wasteful of resources, and can be potentially harmful to patients.

The most common bacteria causing infection are *Staphylococcus aureus* and β-haemolytic streptococci. *Pseudomonas aeruginosa* is frequently found in chronic ulcers, but is rarely the cause of infection. However, it is able to impair host defences by inducing inappropriate or premature apoptosis in macrophages and neutrophils.[2, 3] It interferes with host defences, which delays healing. On occasion, less common but important pathogens are isolated from an ulcer swab. *Pasteurella multocida* is one example; this gram-negative bacillus which is a commensal in the mouth of kittens and cats, is occasionally identified. The likely source is a kitten or cat of the elderly owner licking/desloughing the ulcer, at some point inoculating it with the pathogen! In addition to cellulitis, life-threatening systemic infection can occur.

Wound swabs account for about 10% of the bacteriology specimens received from primary care, and unlike urine and genital swab specimens, there is no significant bias in terms of sex.

86 The chronic leg ulcer swab. An example where a swab is taken where there is a clear evidence of infection. The steps in the process can be divided into seven critical steps (see Chapter 1, 1).

In this scenario, the chronic leg ulcer has surrounding painful cellulitis, and a swab should be taken. The primary care nurse carefully washes the ulcer, and removes some slough to obtain a sample adjacent to viable tissue. The specimen grows group A streptococcus, and the result is telephoned by the laboratory. The primary care physician telephones the patient, who relates that after 24 hours of treatment, the pain and redness is not settling. On discussion with the microbiologist, the decision is made to change to doxycycline, as the organism may be resistant to macrolides; this is confirmed the next day with the susceptibility result. In this example, there was correct management from the outset through to critical step 7, where assessment of the patient after review of the laboratory report prompted the appropriate change of treatment.

Storage and transport of the routine swab from an ulcer or wound

Buffered semi-solid charcoal 'transport swabs' are usually used. The environment in these 'transport swabs' is such that it can maintain the viability of both aerobes and anaerobes for several days, without allowing their multiplication. The swab should be well loaded with as much of the appropriate sample as possible. If there is a delay in transport to the laboratory, the specimen should be refrigerated; viable organisms can be recovered for up to 72 hours at least. Note that if there is pus present/likely to be present, this should be collected as pus, rather than a swab of the fluid. Any pus should be carefully aspirated, and placed in a sterile white-topped container. If there is a delay in transport, the sample should be refrigerated.

86

CRITICAL STEP 1:
Is collection of a specimen indicated?

The Practice team collects a swab from an ulcer of a 75-year-old patient. The skin bordering the ulcer is red and painful. As the patient is penicillin-allergic, a prescription for erythromycin 500 mg q6h and analgesia, is written up.

CRITICAL STEP 2:
Obtain a good quality specimen.

The nurse carefully washes the ulcer with saline to remove surface contaminants and slough with a swab to reveal viable tissue. A fresh swab is taken from this area.

CRITICAL STEP 3:

Record the full patient and clinical details and type of specimen on the request form. Where necessary, record the specific test request.

CRITICAL STEP 4:

How is the specimen stored and what is the frequency of transport to the laboratory?

CRITICAL STEP 5:

What is the quality of the laboratory process, including turnaround times?

CRITICAL STEP 6:

Is immediate or routine reporting of this result required by the laboratory?

The result should be communicated to the practice/clinic now.

CRITICAL STEP 7:
How is the laboratory report interpreted?

Phoned report from microbiology: Profuse growth of group A streptococcus; Sensitivities to follow

Primary care physician telephones the patient. The patient reports that the ulcer is still painful, and there is no reduction in the redness. On discussion with the microbiologist, doxycycline is prescribed. This change is confirmed with the susceptibility profile available the next day

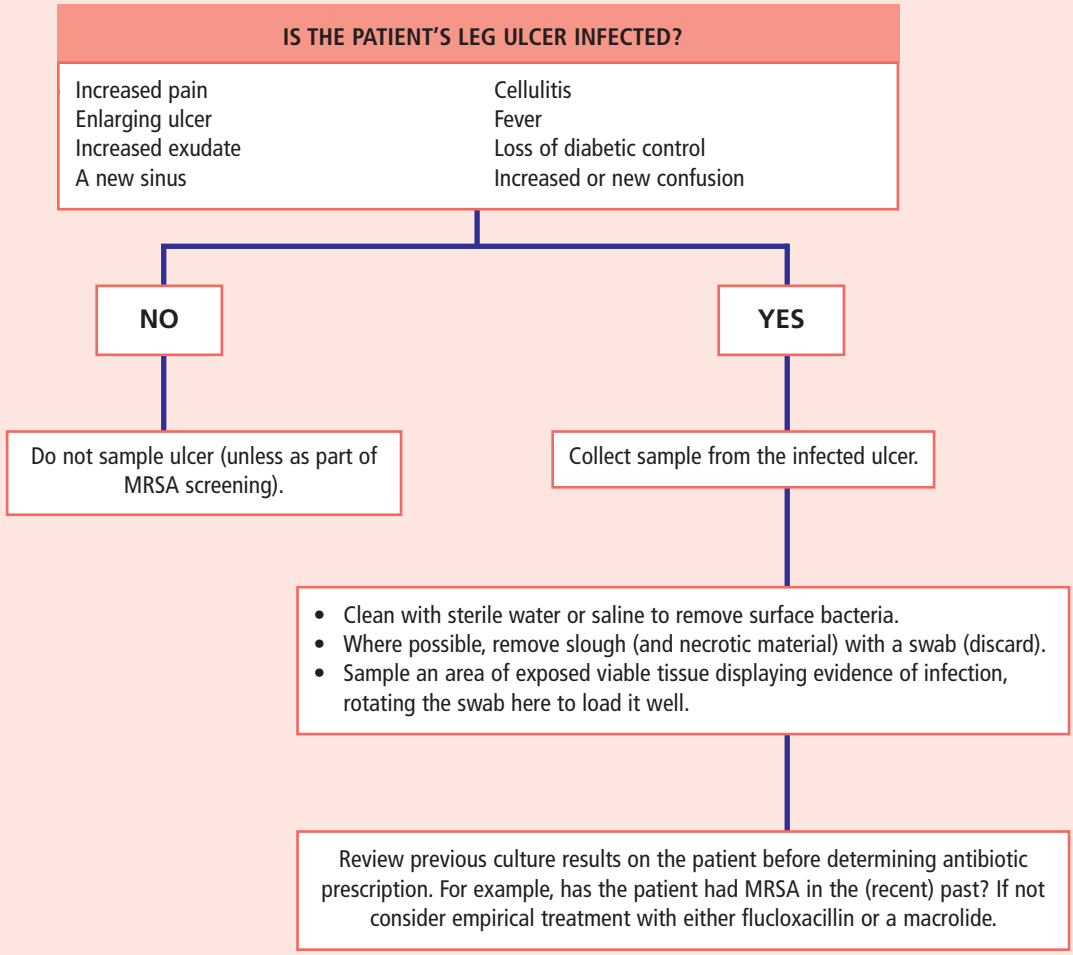
Report on AB, 75-year-old:
Leg ulcer MC&S
Profuse growth of group A streptococcus:

Penicillin	S
Erythromycin	R
Tetracycline	S

Quick Action Guide – 1

The chronic leg ulcer; reviewing the patient at the first visit.

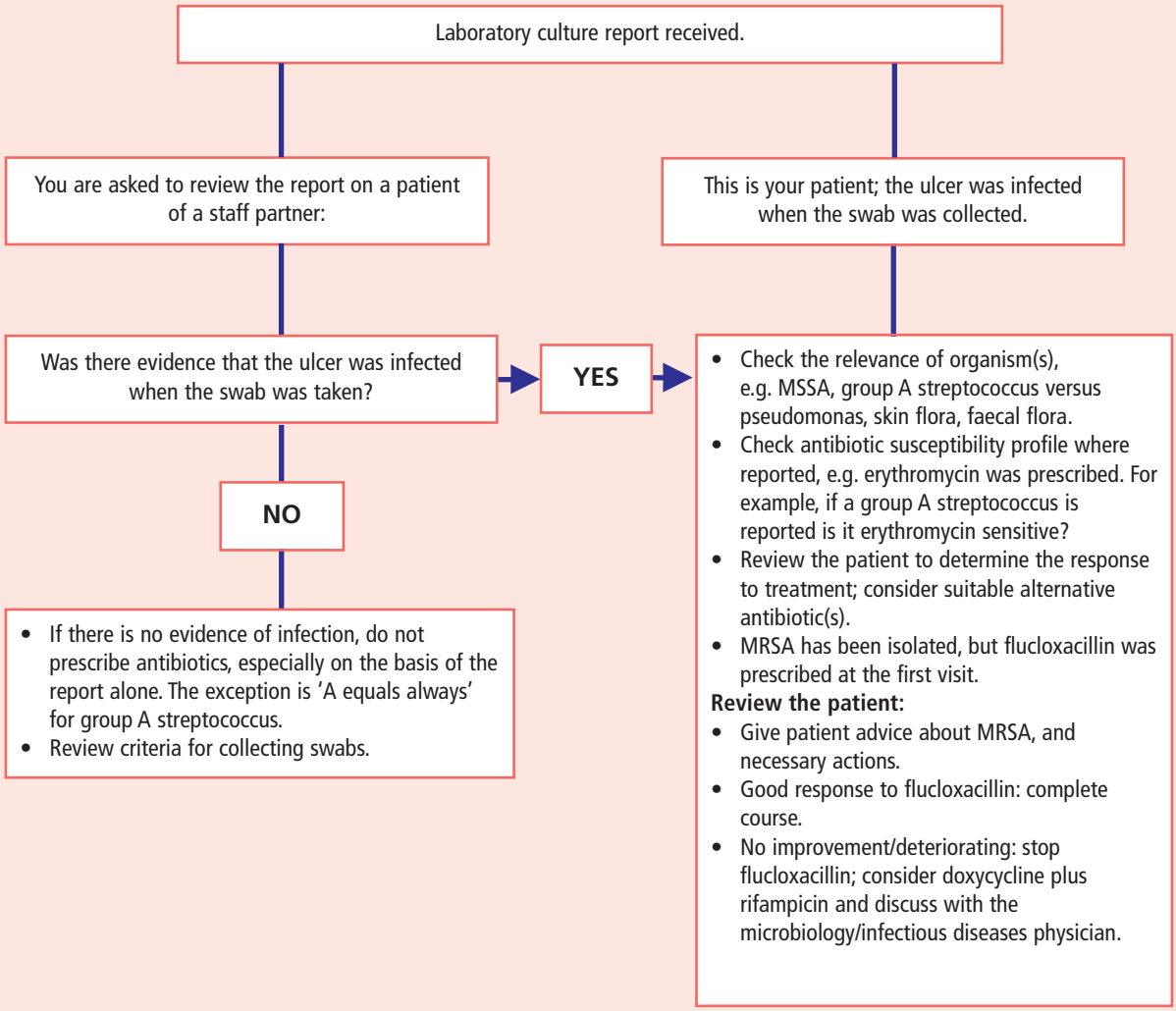
(Adapted in part from *Venous Leg Ulcers: Infection, Diagnosis and Microbiology Investigation; Quick Reference Guide for Primary Care*. www.hpa.org.uk.[1]
With permission of the UK Health Protection Agency.)


IS THE PATIENT'S LEG ULCER INFECTED?
Increased pain
Enlarging ulcer
Increased exudate
A new sinus
Cellulitis
Fever
Loss of diabetic control
Increased or new confusion
NO
YES
Do not sample ulcer (unless as part of MRSA screening).
Collect sample from the infected ulcer.
• Clean with sterile water or saline to remove surface bacteria.
• Where possible, remove slough (and necrotic material) with a swab (discard).
• Sample an area of exposed viable tissue displaying evidence of infection, rotating the swab here to load it well.
Review previous culture results on the patient before determining antibiotic prescription. For example, has the patient had MRSA in the (recent) past? If not consider empirical treatment with either flucloxacillin or a macrolide.

Quick Action Guide – 2

The chronic leg ulcer; reviewing the laboratory report, with the reason for the swab being taken.

(This Quick Action Guide is adapted, in part, from *Venous Leg Ulcers: Infection, Diagnosis and Microbiology Investigation; Quick Reference Guide for Primary Care*. www.hpa.org.uk.[1] With permission of the UK Health Protection Agency.)


Laboratory culture report received.
You are asked to review the report on a patient of a staff partner:
This is your patient; the ulcer was infected when the swab was collected.
Was there evidence that the ulcer was infected when the swab was taken?
YES
NO
• Check the relevance of organism(s), e.g. MSSA, group A streptococcus versus pseudomonas, skin flora, faecal flora.
• Check antibiotic susceptibility profile where reported, e.g. erythromycin was prescribed. For example, if a group A streptococcus is reported is it erythromycin sensitive?
• Review the patient to determine the response to treatment; consider suitable alternative antibiotic(s).
• MRSA has been isolated, but flucloxacillin was prescribed at the first visit.
Review the patient:
• Give patient advice about MRSA, and necessary actions.
• Good response to flucloxacillin: complete course.
• No improvement/deteriorating: stop flucloxacillin; consider doxycycline plus rifampicin and discuss with the microbiology/infectious diseases physician.
• If there is no evidence of infection, do not prescribe antibiotics, especially on the basis of the report alone. The exception is 'A equals always' for group A streptococcus.
• Review criteria for collecting swabs.

87

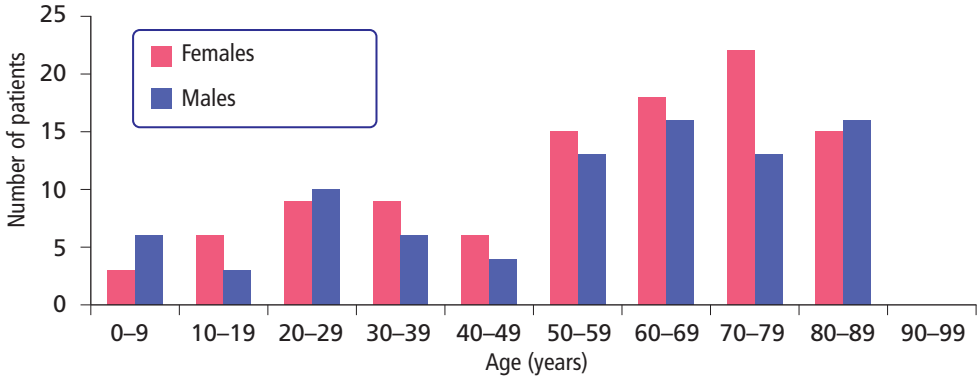
Commonly considered as a pathogen in an infected ulcer, when there is evidence of infection:
Staphylococcus aureus (MSSA or MRSA)
Group A streptococcus
Group C streptococcus
Group G streptococcus

Commonly considered as secondary colonizers, and can be important in the development of critical colonization. They can occasionally be the causative agent:
Pseudomonas aeruginosa
Anaerobes/mixed anaerobes

Colonizers of ulcers with unlikely pathogenic potential:
Coagulase-negative staphylococci
Diphtheroids
Skin flora
'Coliforms'
Escherichia coli (including ESBL-producers)

87 A list of the bacteria that are associated with the infected chronic leg ulcer. See Appendix, Chapter 5 for more detailed information.

88



88 The typical age and sex distribution of patients submitting wound swab specimens to the laboratory over a period of 1 week.

Relatively more swabs are received from individuals over 50 years of age (88). Clinical details include 'Leg ulcer-? infected', (this in itself indicates the swab was taken inappropriately), 'Leg ulcer +++slough', 'Infected post operation wound', and 'Paronychia'. Swabs taken from chronic leg ulcers can account for over 20% of wound swabs submitted to the laboratory, based on the clinical details recorded on the request form.

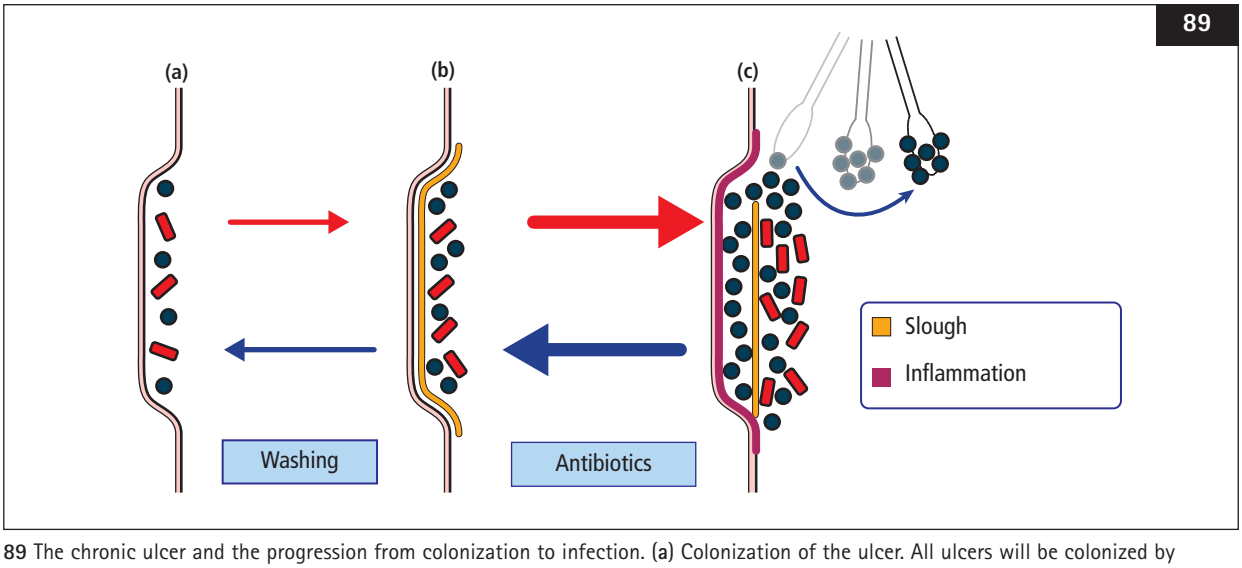
SPECIFIC ISSUES ASSOCIATED WITH THE CHRONIC LEG ULCER SWAB

Colonization versus infection

As highlighted in Chapter 1, differentiating colonization from infection is fundamental in providing correct patient care. This is particularly important in primary care, where apart from the occasional specimen collected from a 'true sterile site' such as a bursa, all others, with the exception

of urines, are collected from sites that have, or pass over, a resident bacterial flora. Careful assessment of the chronic leg ulcer, and making a clinical diagnosis of whether it is infected or not is so important; the result of a microbiology swab cannot determine if there is infection.[4, 5] If a swab is taken unnecessarily or incorrectly, it can initiate a chain of events that waste resources, and by giving antibiotics unnecessarily, can be detrimental to the patient.

Chronic leg ulcers and pressure ulcers will always be colonized with bacteria, as there is a rich source of nutrients supporting biofilm growth, consisting of a mixed population of aerobic, facultative, and anaerobic bacteria. At some stage, the bacterial population in the ulcer progresses to a 'critical colonization' stage.[6] The ulcer looks unhealthy, and is not healing, but there are no obvious signs of infection, either locally or systemically. *Pseudomonas aeruginosa* is considered to play a key role in critical colonization by producing subclinical damage to tissue and consequent delay in healing. As a result biofilm formation, and chronic inflammation stimulated by the organism, may give rise to a Trojan horse effect for other pathogens.[7] In malodorous ulcers, anaerobes such as *Bacteroides* spp. and *Peptostreptococcus* spp. are likely to be present, and can be found in up to 30% of venous ulcers.[8] The critically colonized ulcer can provide the environment for a pathogen such as *Staphylococcus aureus* or group A streptococcus to initiate infection in the ulcer base and edge. The changes from colonization to critical colonization then to infection, and the modalities that can be used to reverse this, are shown in **89**. The key to reducing the chance of critical colonization and thus infection in ulcers is regular washing to remove debris and bacteria. In assessment of the infected ulcer, one needs to consider the depth of infection and whether any deep-seated structures are involved, such as bone which would necessitate specialist referral. (The smell of an ulcer can also be very useful in assessment, as a 'rotten flesh' smell indicates that there is underlying necrosis, and debridement is needed).



89 The chronic ulcer and the progression from colonization to infection. **(a)** Colonization of the ulcer. All ulcers will be colonized by bacteria. Initially various organisms such as CNS, MSSA, and pseudomonas take up residence. **(b)** Critical colonization of the ulcer. Here the bacterial flora has increased to a degree that tissue viability becomes compromised. At this stage, the situation is salvageable. However, if not remedied, it can progress to infection. **(c)** Infection of the ulcer. Local invasion by MSSA occurs, with increased pain, purulent exudate, and surrounding erythema/cellulitis. Correct swabbing samples the pathogen. The progression from the colonized ulcer to critical colonization can be prevented by regular washing with water. Antibiotics have no role here. Appropriate antibiotics given promptly for infection against the most likely pathogen should resolve the situation.

PRIMARY CARE

The key issue in primary care is to have defined guidelines for the care of the patient with chronic leg ulcers, developed in conjunction with the community tissue viability nurse. These guidelines should detail all the aspects of care that can prevent infection in the ulcer, including ulcer washing at regular intervals, and close monitoring of blood glucose in the diabetic patient. There should be clear protocols for when and how to collect swabs, and for interpreting the laboratory report. Of overriding importance is that staff receive ongoing training otherwise such protocols become yet another policy that gathers dust on the shelf.

THE PATIENT

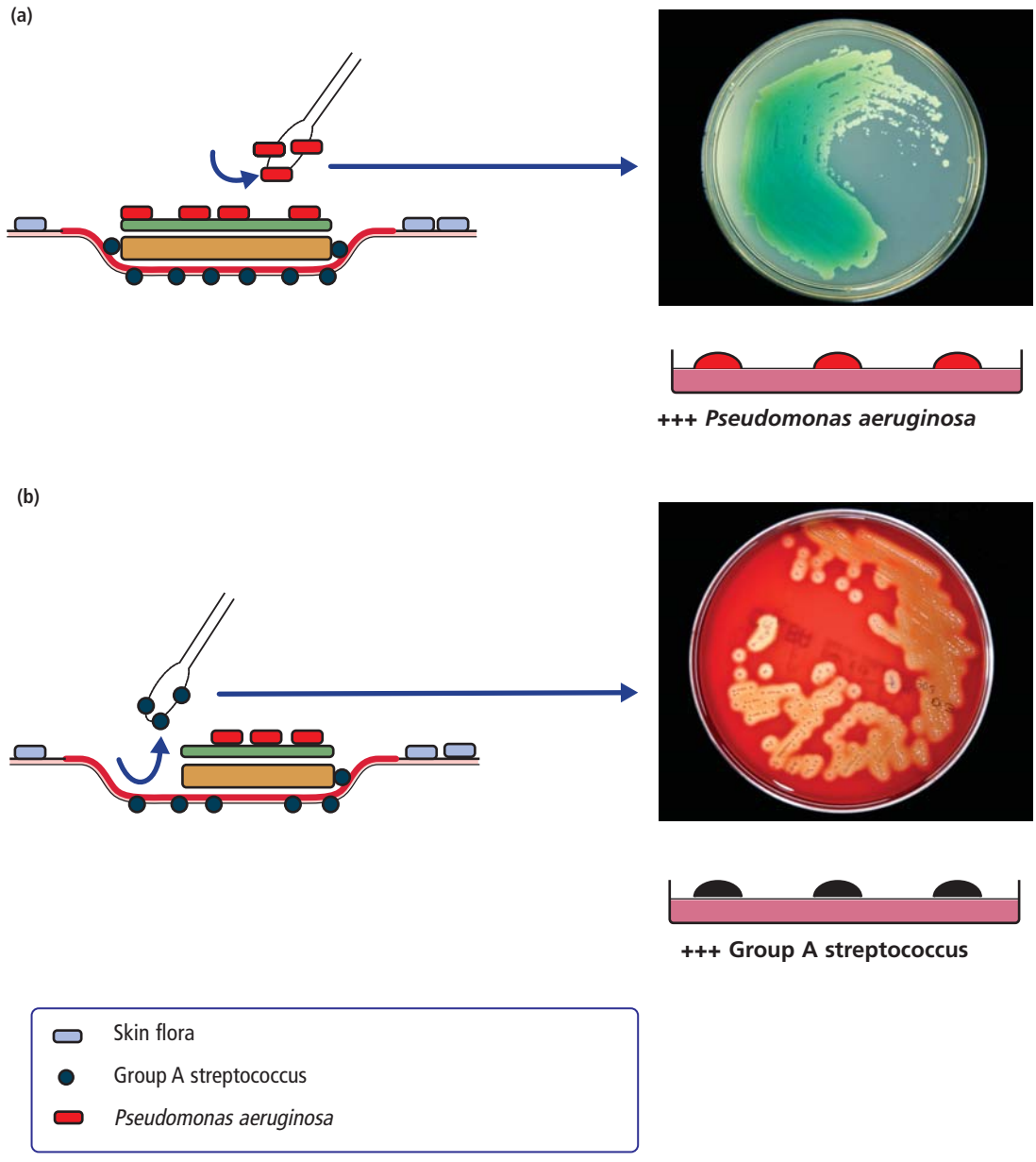
The patient with chronic leg ulcers is usually older, and will often have other co-morbidities such as diabetes and/or peripheral vascular disease. With diabetes, the reaction to infection may be modified, with neuropathy, ischaemia, and a reduced pain response making assessment more difficult. Monitoring full blood count (FBC), C-reactive protein (CRP), and blood glucose can help in decision making. There should be close cooperation with the community tissue viability nurse, the diabetic physician and dermatologist, with a prompt referral system to manage the patient who is not responding to standard treatment. The vascular surgeons would be involved as needed. In order to reduce the 'critical colonization' stage and thus infection, regular washing of the ulcer should be done. A litre of water can be boiled, and when it has cooled, one heaped tablespoon of aqueous cream is mixed into this. The use of aqueous cream is important as it moistens the surrounding skin; dry scaly skin is more likely to be colonized with *Staphylococcus aureus*.

Not infrequently a patient is diagnosed as having bilateral cellulitis. True bilateral cellulitis is uncommon, and conditions such as venous hypertension, or varicose eczema, with associated swelling and skin discolouration, should be considered.[9] This can be improved by leg elevation, compression bandages, and ankle exercises. Increased nonpurulent exudate from ulcers can also be mistaken as infection, and in addition to the interventions above, increasing the frequency of washing the affected limb(s), and of dressing changes is useful. Cellulitis can also be confused with an allergic reaction when there is erythema localized to, and taking the shape of the dressing; this points to an allergic reaction.[9] The likely cause should be removed, and 'patch testing' done as required. Beware of the patient with such conditions who has true cellulitis of one leg.

COLLECTING THE SPECIMEN

When infection is identified, a specimen should be collected using care to choose the area likely to contain the probable pathogen. A swab collected from the superficial layer of the ulcer, where slough or exudate is present is of little use, as the bacteria identified may not represent the organism responsible for the infection. The ulcer area should be washed first with tap water or saline, in order to detach any surface material, such as slough and necrotic material, thus reducing the likelihood of sampling surface contaminants.[10, 11] Where possible, a swab should be used to remove this material, in order to expose viable tissue. A fresh swab should then collect the sample from the infected area, rotating it to maximize the loading (**90**).

90



90 (**a**) Sampling the surface slough of an ulcer will produce a report showing a profuse growth of pseudomonas. A decision to treat with oral ciprofloxacin is incorrect, and puts the patient at risk of CDAD. (**b**) Washing with sterile saline, followed by careful removal of the slough obtains a deeper sample, which grows group A streptococcus, the pathogen.

THE REQUEST FORM

The relevant clinical details should be included on the request form. If methicillin-resistant *Staphylococcus aureus* (MRSA) screening only is required, this information should be clearly visible to the laboratory staff. In order to readily identify MRSA, a selective agar medium is used that prevents the growth of most other bacteria, including other pathogens; the standard microscopy, culture, and sensitivity (MC&S) cannot be done. Any relevant history of travel, exposure to water (fresh or sea) should be given. While *Vibrio vulnificus* is often a rapidly progressing infection, other marine vibrios, such as *Vibrio alginolyticus* can also cause skin and soft tissue infection. This information is a useful guide for the laboratory staff.

THE LABORATORY REPORT

The key point when reviewing the report is firstly to confirm if the swab was taken for the correct reason, i.e. clinical evidence of infection. Only if this is the case should one proceed to correlate this with the bacteria reported and the antibiotics prescribed. Quick Action Guide 2 should be referred to.

Interpreting a report can be difficult if the primary care physician has not seen the patient, unless clear clinical reasons have been recorded in the patient's record. As a minimum, assessing whether there were signs of infection, and the appropriateness of the antibiotics should be confirmed; **91** gives guidance. If the result showed that methicillin-sensitive *Staphylococcus aureus* (MSSA), group A, group C, or group G streptococcus was isolated, and flucloxacillin was given, all four bacteria would be susceptible to this agent. If MRSA was isolated, prompt review of the patient would be needed. The infection may in fact have improved, with the flucloxacillin treating a susceptible pathogen, indicating that MRSA was a colonizer! If there is no improvement, doxycycline can be given to treat the MRSA; rifampicin can be added as a second agent. (Also see Chapter 2, **33**, **34**).

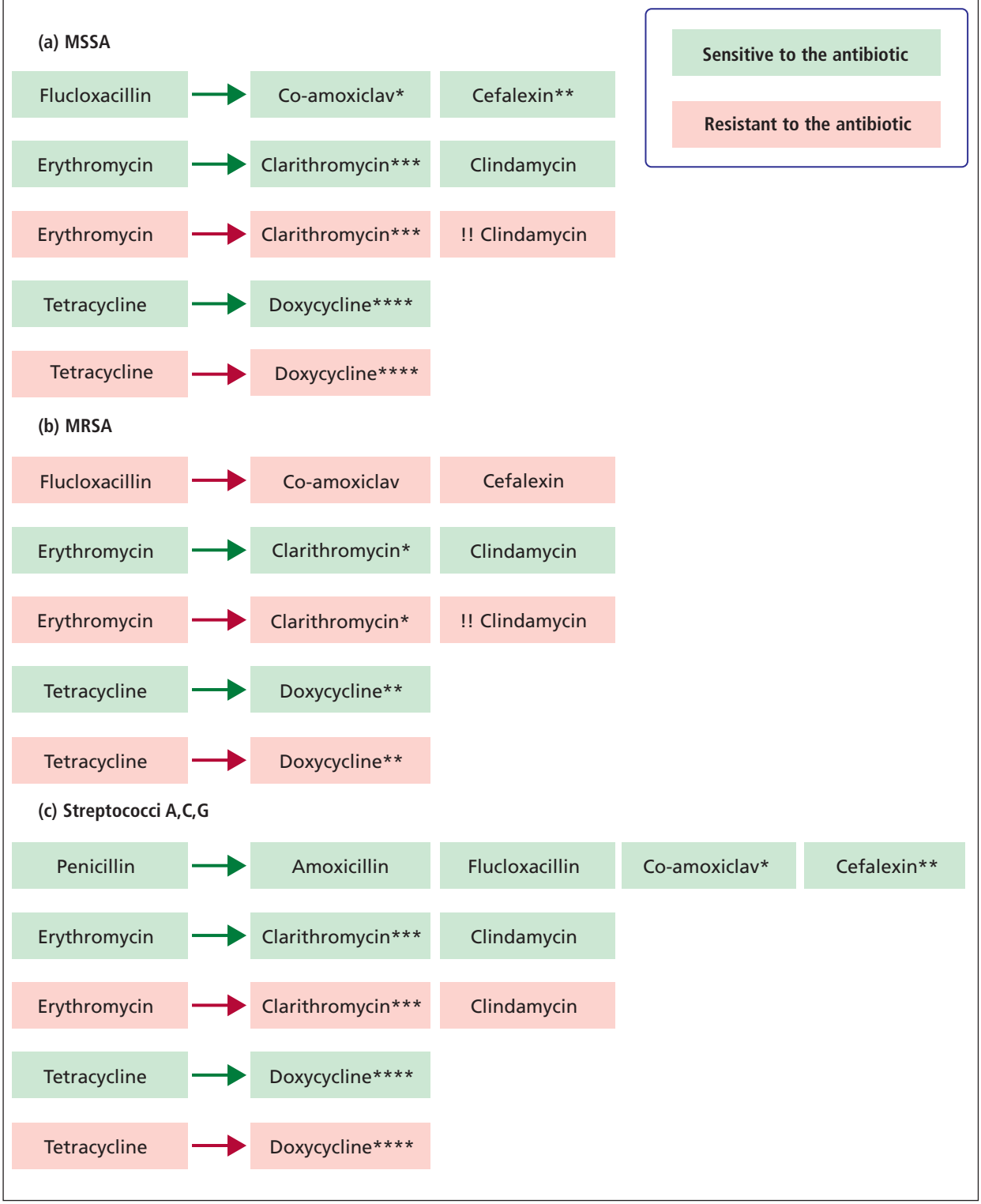
91 The laboratory will report a limited number of antibiotics for organisms such as MSSA, MRSA, and streptococci. The appropriateness of the antibiotic prescribed should be reviewed with the information in this Figure, which shows the susceptibility of the organism to other agents as well (See Chapter 2, **33** and **34**). In the diagram, left panels are the laboratory report showing the susceptibility of the organism, and right (arrowed) panels other agents to which the organism will either be sensitive or resistant.

(a) With MSSA, flucloxacillin, erythromycin, and tetracycline should be reported by the laboratory as a minimum.
*Co-amoxiclav is broader spectrum than flucloxacillin, and for an infected leg ulcer only, it would be reasonable determine why this was prescribed, and to consider changing the treatment to flucloxacillin.
**A cephalosporin, such as cefalexin, can be given in the penicillin-allergic patient, when the nature of the allergy allows the use of a cephalosporin. There is a CDAD risk to consider, but this is a useful option, when for example the organism is resistant to both erythromycin and tetracycline, and when the benefit is considered to outweigh the risk.
***This includes the other macrolides.
****This includes the other tetracyclines.
(‼: Note that some laboratories test, and then report clindamycin separately for *Staphylococcus aureus*; a proportion of organisms that are resistant to erythromycin are clindamycin sensitive.)

(b) With MRSA, flucloxacillin, erythromycin and tetracycline should be reported as a minimum. If the organism is resistant to erythromycin and/or tetracycline, the laboratory should 'release' another antibiotic, such as trimethoprim or co-trimoxazole (TMP - SMX).
*This includes the other macrolides.
**This includes the other tetracyclines.
(‼: Note that some laboratories test, and then report clindamycin separately for *Staphylococcus aureus*; a proportion of organisms that are resistant to erythromycin are clindamycin sensitive.)

(c) For group A, C, and G streptococci, penicillin, erythromycin, and tetracycline should be reported by the laboratory.
*Co-amoxiclav is broader spectrum than amoxicillin (and flucloxacillin), and for an infected leg ulcer only, it would be reasonable to determine why this was prescribed, and to consider changing the treatment to amoxicillin.
**A cephalosporin, such as cefalexin, can be given in the penicillin-allergic patient, when the nature of the allergy allows the use of a cephalosporin. There is a CDAD risk to consider, but this is a useful option, when for example the organism is resistant to both erythromycin and tetracycline, and when the benefit is considered to outweigh the risk.
***This includes the other macrolides.
****This includes the other tetracyclines.

91


Sensitive to the antibiotic
Resistant to the antibiotic
(a) MSSA
Flucloxacillin
Co-amoxiclav*
Cefalexin**
Erythromycin
Clarithromycin***
Clindamycin
Erythromycin
Clarithromycin***
!! Clindamycin
Tetracycline
Doxycycline****
Tetracycline
Doxycycline****
(b) MRSA
Flucloxacillin
Co-amoxiclav
Cefalexin
Erythromycin
Clarithromycin*
Clindamycin
Erythromycin
Clarithromycin*
!! Clindamycin
Tetracycline
Doxycycline**
Tetracycline
Doxycycline**
(c) Streptococci A,C,G
Penicillin
Amoxicillin
Flucloxacillin
Co-amoxiclav*
Cefalexin**
Erythromycin
Clarithromycin***
Clindamycin
Erythromycin
Clarithromycin***
Clindamycin
Tetracycline
Doxycycline****
Tetracycline
Doxycycline****

If the report states growth of a 'coliforms', pseudomonas, or faecal flora, and the infection has improved, for example with flucloxacillin, there is no need to take further action. It is likely that the antibiotic has treated an underlying MSSA or β-haemolytic streptococcus, which was not sampled and subsequently cultured because of poor collection. If there is no improvement, appropriate resampling of the ulcer would be indicated as well as discussing any empirical treatment pending the result with a medical microbiologist/infectious diseases physician.

TREATMENT

The Antibiotic Guidelines in Chapter 11 gives more details of common antibiotic regimes used in the community. It is useful to refer to **91** again, as this discusses further options to consider in the penicillin-allergic patient, based on the antibiotic susceptibilities reported.

SUMMARY AND KEY POINTS

This chapter is mainly concerned with the wound swab in the setting of chronic leg ulcers. The same principles of colonization and infection apply to post-surgical wounds, with specimen collection and treatment only undertaken when there is evidence of infection. Following cardiothoracic, orthopaedic, or neurosurgical procedures, it is important to contact the specialist team promptly by telephone if the patient has evidence of anything more than a minor infection at the operation site.

In summary, the following points must be noted:

- The practice/clinic should establish a set of guidelines for clinical and nursing staff to use so that there are set criteria, centred on Quick Action Guides and the critical steps of **86**.
- These should be used regularly as a training tool to give guidance on when and how to collect specimens from the various patient age groups, storage and transport of specimens, and how the laboratory report should be interpreted.
- It is essential to be familiar with the principles of colonization and infection. Sampling any superficial wound should only be done where there is clear evidence of infection. Highlighting this will save valuable resources in the practice/clinic and laboratory. (Essentially the only other requirement for swabbing is MRSA screening pre-hospital admission.)
- The laboratory report must be interpreted in light of the organisms identified, and thus distinguish likely pathogens from bacteria colonizing the ulcer. This will prevent unnecessary and incorrect antibiotic prescribing.
- Patients who are MRSA-positive should be told to inform staff at any other health-care centre they may attend of their MRSA status.

6
Fungal Scrapings of the Nail Apparatus (Onychomycosis), the Hair, and the Skin

- Introduction
- Organisms and epidemiology
- Specific issues with the fungal scraping specimen
- Primary care
- The patient
- Collecting the specimen
- The request form
- The laboratory report
- Treatment
- Summary and key points

INTRODUCTION

This chapter highlights three key points to consider in managing the patient who is being investigated for a fungal infection of the nails, skin, or hair.

The key points are:

- Knowing when to collect a dermatophyte specimen.
- Ensuring that a good quality specimen is collected, and transported to the laboratory in a manner that minimizes contamination and overgrowth of bacteria.
- Knowing how to interpret the report.

Figure **92** and the Quick Action Guides expand on these key issues, and should be used as a training tool to emphasize the critical steps relevant in primary care.[1]

ORGANISMS AND EPIDEMIOLOGY

Fungal infections of the skin, hair, and nails are common, and are caused primarily by the dermatophyte moulds (**93**, page 102).[2] These organisms grow on the stratum corneum, which consists of flattened, fused skin cell remnants, made up of the fibrous protein, keratin. The source of the organisms is either human, animal, or from soil; there are three genera, *Epidermophyton*, *Microsporum*, and *Trichophyton*.

Skin infections are labelled 'tinea', a derivation of the Latin term for 'moth eaten', and are related to the parts of the body where the infection occurs. These are: tinea capitis (the scalp), tinea barbae (the beard), tinea corporis (the body), tinea unguinum (the nails; onychomycosis), tinea manuum (the hands), tinea pedis (the feet), and tinea inguinalis (the groin). This latter entity should not be referred to as tinea cruris, as cruris relates to the leg. The alternative inclusive term for these infections is 'ringworm'. Nondermatophyte moulds such as aspergillus and scopulariopsis, as well as yeasts can cause infections of the skin and nails.

Certain dermatophyte infections are more common in different age groups. Scalp ringworm is found in children, but seldom persists beyond 16 years of age, whereas athlete's foot often begins in late childhood, and is more frequent between the ages of 20 and 50 years, where there is often current infection of the groin as well, particularly in males.[3] Dermatophytes are acquired from other humans (anthropophilic), either directly or indirectly, from animals such as cats, dogs, and rodents (zoophilic), or, uncommonly, from the soil (geophilic), where farm workers and gardeners may be exposed to these fungi.[4] Anthropophilic dermatophyte infections, such as those of the toes and feet, are acquired by contact with infected desquamated skin scales. They are typically acquired in damp communal environments, such as swimming pools and any other shared bathing area. Inadequate drying of the toes allows the infection of tinea pedis ('athlete's foot') to become established, resulting in for some individuals a chronic and distracting infection; there may be a genetic susceptibility to this infection. Fungi such as *Scopulariopsis brevicaulis* can be considered as 'secondary invaders', and infect toe nails that are dysmorphic, having been damaged by preceding or ongoing infection caused by a dermatophyte such as trichophyton.

92 The dermatophyte specimen. An example where the patient is allowed to collect a specimen, which should be done instead by trained staff. The specimen is subsequently stored incorrectly. The steps in the process can be divided into seven critical steps (see Chapter 1, 1).

In this scenario, critical step 2 is breached, as the patient is asked to collect the specimen. For dermatophyte infections of the nail, scalp, or skin, specimens must be collected by the primary care physician or nurse, and not the patient. Critical step 2 is breached when the inappropriate specimen container is used. Critical step 4 is breached, when the sample is stored in the practice/clinic refrigerator, keeping the specimen damp. During transport bacteria multiply at room temperature, and have the potential to overgrow the fungus.

Storing and transport of the nail, hair, and skin specimen for dermatophyte examination

Skin scrapings, scalp scrapings with hairs/hair roots, and nail clippings/nail debris should be collected into a designated container for dermatophyte examination such as in the UK, the Dermapak®. (The black background helps the laboratory staff to see the material easily.) Once taken, these dry specimens must be stored and transported at room temperature. Specimens must not be refrigerated, as cooling can inhibit the growth of the fungi, and any humidity allows subsequent overgrowth of bacteria during transport and before processing in the laboratory, reducing the likelihood of growing the fungus, even on the selective medium used.

92

CRITICAL STEP 1:
Is the collection of a specimen indicated?

The patient with chronic nail infection is asked by the primary care team to collect nail clippings.

CRITICAL STEP 2:
Obtain a good quality specimen.

No advice is given to the patient, who cuts nail material after showering when nails are soft and easy to cut. The specimen, placed in folded paper by the patient, is received in the practice/clinic on Friday evening and is refrigerated until Monday morning.

CRITICAL STEP 3:

Record the full patient and clinical details on the request form. Where necessary, record the specific test request.

CRITICAL STEP 4:

How is the specimen stored; note that for dermatophytes, specimens should not be refrigerated. What is the frequency of transport to the laboratory?

CRITICAL STEP 5:

What is the quality of the laboratory process, including turnaround times?

CRITICAL STEP 6:

Is immediate or routine reporting of this result required by the laboratory?

CRITICAL STEP 7:
How is the laboratory report interpreted?

Report on AB, 65-year-old. Nail clippings for dermatophyte investigation:
Microscopy: Fungal elements NOT seen
Fungal culture: Overgrown with contaminants

The patient is called to inform him that there is no positive result to use in management of the condition.

Repeat specimens have to be collected by the primary care nurse, necessitating additional use of primary care and laboratory resources, and inconveniencing the patient.

Quick Action Guide – 1

Fungal scrapings of the nail apparatus (onychomycosis), the hair, and the skin

(*Fungal Skin and Nail Infections: Diagnosis and Laboratory Investigation; Quick Reference Guide for Primary Care.*[1] Adapted in part with permission of the UK Health Protection Agency.)

When and how to collect specimens for the identification of dermatophytes:

Clinical examination shows uncomplicated athelete's foot, mild infection of the groin or skin (ringworm).

Give advice to patient about foot, groin, and skin care, ensuring skin is dry and well aired after bathing or swimming. Recommend topical antifungal agent.

No response

Scalp ringworm, nail disease, extensive skin infection, failure to respond to treatment, or diagnosis uncertain.

Collect specimen for laboratory examination.

Have appropriate sample container, e.g. Dermapak® ready to place sample in.

The skin and/or nail area should be clean and dry, and any lotions or treatment creams must be wiped off.

As over 90% of diagnoses are based on microscopy, a relatively insensitive method, sufficient sample must be collected; for skin scrapings this should fill a volume of at least 5 mm^3.

Skin:

- Scrape skin outwards towards the advancing edge of the lesion, using a blunt scalpel blade held perpendicular to the skin.

Nail:

- **Sample all the debris from under the nail,** then clip full thickness nail up to most proximal and lateral part of the nail that can be removed which is comfortable for the patient.
- For superficial and proximal white onychomycosis, scrape from the diseased surface of the nail.

Hair:

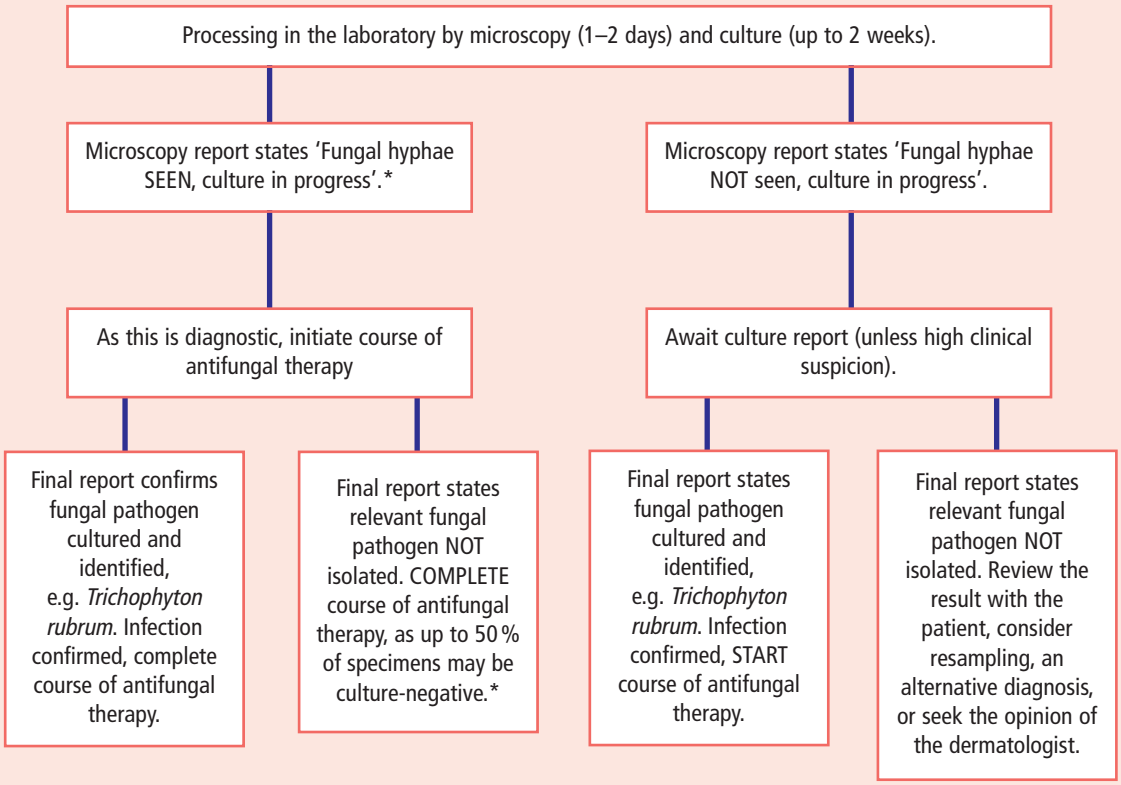
- Collect scalp scrapings which pull out clumps of hair stumps, which are important for successful microscopy and culture.

Seal sample container, complete full details on the outside, and full clinical details on the form, including animal contacts, the immunocompromised patient.

Transport to the laboratory. Keep samples at room temperature, as cooling inhibits dermatophyte growth, and humidity encourages overgrowth of bacteria.

Quick Action Guide – 2

The interpretation of the laboratory report


Processing in the laboratory by microscopy (1–2 days) and culture (up to 2 weeks).
Microscopy report states 'Fungal hyphae SEEN, culture in progress'.*
Microscopy report states 'Fungal hyphae NOT seen, culture in progress'.
As this is diagnostic, initiate course of antifungal therapy
Await culture report (unless high clinical suspicion).
Final report confirms fungal pathogen cultured and identified, e.g. Trichophyton rubrum. Infection confirmed, complete course of antifungal therapy.
Final report states relevant fungal pathogen NOT isolated. COMPLETE course of antifungal therapy, as up to 50 % of specimens may be culture-negative.*
Final report states fungal pathogen cultured and identified, e.g. Trichophyton rubrum. Infection confirmed, START course of antifungal therapy.
Final report states relevant fungal pathogen NOT isolated. Review the result with the patient, consider resampling, an alternative diagnosis, or seek the opinion of the dermatologist.

*Microscopy is an insensitive technique. Therefore, if fungal elements are seen, they must be present in high numbers, and hence this is diagnostic of infection. About 50 % of specimens may be culture-negative despite positive microscopy. This reflects the difficulties with culture, and does not invalidate the initial diagnosis based on microscopy.

93

Dermatophytes

Epidermophyton floccosum	Human	Cause of tinea inguinalis worldwide. Less commonly, also infects skin and nails of hands and feet.
Microsporum audouinii	Human	Significant cause of ectothrix tinea capitis in children in Central and West Africa, and the Americas. (Ectothrix growing on the outside of the hair.)
Microsporum canis	Cat, dog	Tinea capitis and tinea corporis.
Microsporum gypseum	Soil	Occasional cause of tinea corporis and ectothrix tinea capitis.
Microsporum fulvum	Soil	Occasional cause of human infection.
Microsporum persicolor	Soil	Associated with dogs and rodents. Occasional cause of tinea corporis and tinea manuum.
Trichophyton equinum	Horse	Occasional cause of tinea corporis and tinea capitis.
Trichophyton erinacei	Hedgehog, dog	Uncommon cause of tinea corporis.
Trichophyton interdigitale	Human	Common cause of tinea pedis and tinea unguinum.
Trichophyton mentagrophytes	Many animals, esp. rodents	Cause of tinea corporis, tinea pedis, and tinea capitis.
Trichophyton rubrum	Human	Common cause of tinea pedis, tinea corporis, tinea manuum, and tinea unguinum
Trichophyton schoenleinii		Cause of favus in humans, commonest in North Africa, the Middle East and parts of southern and eastern Europe. There is scalp hair invasion, as well as scalp crusting.
Trichophyton soudanense	Human	Common in Africa. Causes tinea corporis and endothrix tinea capitis.
Trichophyton terrestre	Soil	Not usually pathogenic, but can contaminate skin and nail.
Trichophyton tonsurans	Human	Common in the Americas. Causes tinea corporis and endothrix tinea capitis.

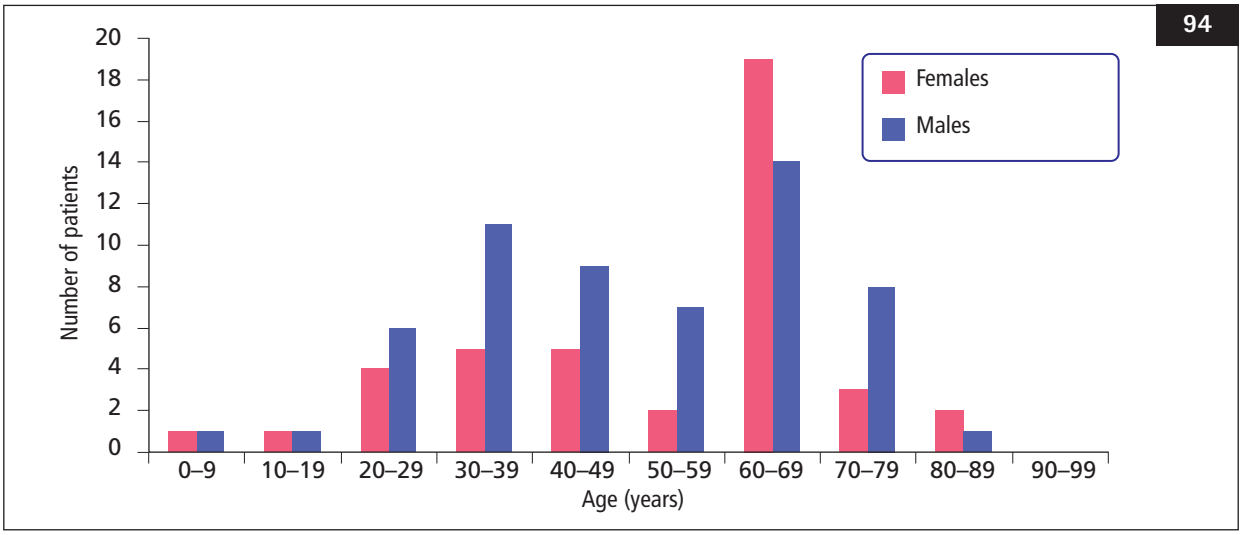
Non-dermatophyte moulds

Acremonium spp.	Environment	Environmental contaminant, but may cause white onychomycosis.
Aspergillus niger	Environment	Common cause of otomycosis.
Aspergillus terreus	Environment	Cause of onychomycosis and otomycosis.
Fusarium spp.	Soil, potato	Environmental contaminant, but can cause white onychomycosis. Can also be an important cause of disseminated infection in immunosuppressed patients.
Penicillium spp.	Environment	Penicillium is not significant. (Note however that *Penicillium marnefii*, found in the Far East is associated with severe infection in the immunocompromised, and is an AIDS defining illness in HIV infection.)
Scopulariopsis brevicaulis	Environment	Onychomycosis. This organism is opportunistic, and invades damaged nails, secondary to a true dermatophyte; it does not colonize healthy nails. Treatment for a dermatophyte should be given first, and itraconazole may be successful. Nail ablation with 40% urea is usually required however.

Yeasts

Candida spp.	'Normal flora'	Candida accounts for 5–10% of all cases of onychomycosis, causing nail fold (paronychia) and distal nail infection. Not surprisingly, fingers are more commonly involved than toes.
Malassezia furfur	Environment	Cause of the superficial infection, pityriasis versicolor. This yeast is difficult to grow in routine culture in the laboratory.
Rhodotorula spp.	Environment	Common contaminant of skin and nails.
Saccharomyces cerevisiae	Environment	With finger nails, can be associated with paronychia.
Trichosporon beiglii	Environment	Cause of the mild hair infection, white piedra.

93 A list of the fungi that are associated with infections of the skin, nails, and hair.[2] See Appendix, Chapter 6 for more detailed information.



94 The typical age and sex distribution of patients submitting specimens for dermatophyte examination to the laboratory over a 1 week period.

Yeasts of the genus *Candida* colonize moist areas of the body (intertrigo), and also cause paronychia of the nails. Paronychia occurs in individuals whose hands are regularly immersed in water; washing and catering are relevant professions. The infection also occurs in nursing mothers, with frequent immersion of the hands in water.[5] Addressing the circumstances that give rise to candidal skin infections, such as the use of waterproof gloves will often solve the problem. More details of common conditions are given at the end of the book (see Appendix).

Examination of consecutive request forms, from specimens for dermatophyte investigation from the community, on the basis of age and sex of the patient, shows that these infections are primarily submitted by adults (**94**). Of these, investigation for onychomycosis (infection of the nail apparatus) is the commonest request. This information reflects the fact that 'ringworm' is usually a clinical diagnosis, whereas the diagnosis and management of scalp and nail infection require submission of a specimen to the laboratory for confirmation.

Lesions caused by athlete's foot can be a portal of entry for organisms such as group A streptococcus, and the toes should be examined for athlete's foot in the patient with cellulitis of the foot and/or lower leg.

SPECIFIC ISSUES WITH THE FUNGAL SCRAPING SPECIMEN

With reference to the critical steps in **92**, and the Quick Action Guide, the following points should be considered in the patient with a dermatophyte infection:

- The need to collect a specimen (1) in nail and scalp infection when oral treatment is being considered, (2) in severe or extensive skin disease, (3) when skin infection is refractory to treatment, (4) or the diagnosis is uncertain.
- **For nail infections, subungual debris (best specimen) as well as full thickness sampling of the most proximal part of the diseased nail must be collected.**
- The correct method of storage and transport of the specimen.
- The correct interpretation of microscopy and culture results.
- Successful treatment regimes are often prolonged.
- Clinical success is not 100 %.

The HPA guidelines[1] states that many nail problems such as psoriasis or trauma resemble fungal infection. It is thus appropriate to send samples before starting lengthy treatment. However, only 45% of these will be positive for fungi, and of these 91 % are detected by microscopy, which also provides the most rapid diagnosis.[6] It is thus essential to obtain a good sample when collecting the specimen. If the clinical diagnosis is not confirmed, and improvement does not occur, it is impossible to determine if this represents treatment failure or an initial incorrect diagnosis.[7]

PRIMARY CARE

There should be suitable equipment available to collect specimens. In addition to chiropody scissors, scalpels and dental scrapers should be available. Reusable equipment must be appropriately decontaminated and sterilized. In addition, there should be stock of a suitable specimen container for dermatophyte specimens, such as Dermapak (www.dermapak.com) and Mycotrans (mail@mycotrans.com).

THE PATIENT

It is not the role of the patient to collect the specimen. The patient should attend with clean dry feet and no topical agents applied to the area.

COLLECTING THE SPECIMEN

The affected area should be clean and dry, and any creams or lotions that have been applied to an affected area must be removed. Specimens for examination in the laboratory must then be collected in the appropriate sample packing systems, such as Dermapak® in the UK (**95–97**).

As nail infection is primarily a disease of the nail bed, rather than the nail plate, subungual debris collected from the most proximal part of the infection is the best specimen. The nail should then be cut back as far as possible and placed in the container. Chiropody scissors and a small dental scraper are useful. Superficial white onychomycosis, usually of the toenails is mainly caused by *Trichophyton mentagrophytes* var. *interdigitale*. Starting as a superficial infection, it spreads to the deeper layers of the nail, and can involve the entire nail plate. The white and flaky surface of the nail plate should be scraped to obtain material for examination. For skin and scalp infections, a scalpel should be used to collect material, which in the case of the scalp must include hair clumps and roots. As much material as possible should be collected in order to maximize the chance of recovering the pathogen. As a general guide, about 5 mm^3 is a useful minimum volume of material to collect. Some points to consider when collecting the specimen are shown in **98**.

THE REQUEST FORM

Clinical details should include any contact with animals and any relevant country of origin or foreign travel, as this can aid the laboratory when identifying the organism on culture. For example, *Trichophyton verucosum* is associated with cattle ringworm, and *Trichophyton soudanese* and *Trichophyton youandei* are common in central and west Africa.[4]

THE LABORATORY REPORT

While microscopy results should be available within several days, culture takes longer as dermatophyte are slow growing, requiring culture plates to be incubated for up to 2 weeks before a final report is issued. It is important to review the microscopy report. About 50 % of all positive specimens are positive for both microscopy and culture, the remainder are positive for microscopy alone. As microscopy is an insensitive technique, observing fungal elements is diagnostic of clinical infection. The reason for culture only being positive in approximately 50 % of cases where fungal elements are seen is thought to be due to the organisms often being in a poor state, or nonviable as they have used up all the nutrients within the sampled nail material by the time of collection.

Laboratories usually report as follows:

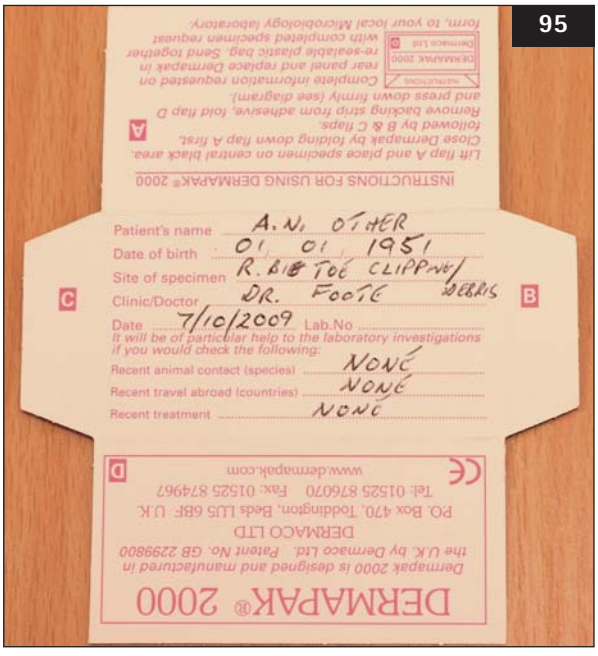
Microscopy: Fungal *elements* SEEN/not seen (Issued as an interim result)
Culture: Fungal *species* ISOLATED/No growth (Issued as a final result)

A positive microscopy result is diagnostic and, if not already started, treatment should be initiated. Likewise, a positive culture but negative microscopy result should prompt treatment. For the reasons given above, a positive microscopy with negative culture result is still diagnostic of infection. If the specimen is negative for both microscopy and culture, this does not rule out fungal infection, particularly with nail infections. If the clinical appearance is very suggestive of fungal infection, a further sample should be collected, and treatment initiated. Comments about overgrowth with bacterial contaminants indicate that the specimen was not collected appropriately.

TREATMENT

Treatment of these fungal infections is given in the antibiotic guidelines (Chapter 11). This is enlarged upon in the individual sections of common conditions given in the Appendix.

Treatment of fungal skin infections is largely based on topical agents, such as clotrimazole and miconazole; systemic agents such as terbinafine and griseofulvin can also be used. Systemic treatment is usually required for infections of the hair and nails as this is the only way to deliver therapeutic levels of the antifungal into the tissue of the growing nail or hair. Because nails are slow growing, treatment of onychomycosis is prolonged, up to 6 months for infections of toenails. Terbinafine and itraconazole have largely replaced griseofulvin, as they have fewer side-effects and are better tolerated. Because therapeutic levels of itraconazole can remain in keratinous tissues for up to 3–4 weeks after stopping treatment, pulsed regimes of a 1-week prescription followed by a 3-week drug-free period


95
Patient's name A.N. OTHER
Date of birth 01 01 1951
Site of specimen R. BIG TOE CLIPPING/DEBRIS
Clinic/Doctor DR. FOOTE
Date 7/10/2009 Lab.No
It will be of particular help to the laboratory investigations if you would check the following:
Recent animal contact (species) NONE
Recent travel abroad (countries) NONE
Recent treatment NONE
DERMAPAK® 2000
Dermapak 2000 is designed and manufactured in the U.K. by Dermaco Ltd. Patent No. GB 2299800
DERMACO LTD
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Tel: 01525 876070 Fax: 01525 874967
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95–97 Designated containers should be used for collecting and transporting dermatophyte specimens. (**95**) The Dermapak® envelope is one example. (**96**) The specimen will be clearly seen against the black background when the envelope is opened in the laboratory. (**97**) After obtaining the specimen, it is sealed into the envelope for transport. Specimens must NOT be refrigerated.

98 Collecting the dermatophyte specimen. A case of severe 'athelete's foot', with inter digit fissuring and bleeding and nail infection. Taking into account the comfort of the patient, debris under the nails, as well as full thickness nail clippings should be collected (arrow). Here significant debris was also scraped off the skin with a scalpel. (When a superficial nail infection is present, scrapings of the nail surface are collected; arrowhead.) Note the specimen collection envelope in the background.

can be used. Itraconazole is the most effective agent for the treatment of candida onychomycosis where the nail plate is invaded. The same regimen that is used for dermatophytes is appropriate (200 mg q12h for 7 days, then 21 days without treatment, repeated for 2 further 28-day cycles). While candidal infection of the toenail is less common, 3–4 cycles of the above regimen can be used.

Where the infection is associated with damp or wet conditions, such as candida paronychia, or athelete's foot, careful drying of the skin after washing is essential. The individual who has infection of the groin should wear loose fitting boxer shorts at home, so the groin area is well ventilated, and kept dry. The use of 'ice cooling' ether-based sprays containing an antifungal such as miconazole can give considerable relief from the distracting discomfort of athlete's foot.

SUMMARY AND KEY POINTS

Although dermatophyte infections may seem trivial, they are a significant cause of medical consultation and absence from work.[8] Athlete's foot can provide a portal of entry for other organisms giving rise to cellulitis and further compromise the limb of those with diabetes or peripheral vascular disease. In patients of any age with cellulitis of the lower limb, history and examination for athlete's foot is important so the predisposing factor can be treated and removed.

The high prevalence of disease is often the result of communal bathing areas being heavily contaminated with the organism. As disinfections of these public areas is impossible, every effort should be made to treat the infection.[9]

In summary, the following points should be noted:

- The practice/clinic should establish guidelines for clinical and nursing staff to use so that there are set criteria, centred on the Quick Action Guides and critical steps of **92**.
- These should be used regularly as a training tool to give guidance on when and how to collect specimens, their storage and transport.
- When interpreting the laboratory report, it is important to appreciate the role that both microscopy and culture have in the diagnosis of dermatophyte infections. Interpreting the report must be part of the training guidelines.

7
The Faecal Specimen

- Introduction
- Organisms and epidemiology
- Specific issues with the faecal specimen
- Primary care
- The patient
- Collecting the specimen
- The request form
- The laboratory report
- Treatment
- *Clostridium difficile* and CDAD
- Hygiene practices
- Summary and key points

INTRODUCTION

This chapter highlights five key points to consider in managing the patient who is being investigated for infectious diarrhoea. These are:

- The clinical assessment of the patient, advice on oral rehydration and personal hygiene, and the need for the patient to inform their employer's occupational health department.
- Recognizing if this is likely to be part of a food-borne outbreak, and if so the need for the primary care physician to inform the local public health department promptly.
- Understanding that relevant clinical details on the request form will alter the range of pathogens investigated in the faecal specimen.
- Giving the patient advice on how to collect a specimen.
- Recognizing that *Clostridium difficile* is an important entity in the community with a specific management strategy.

Figure **99** and the Quick Action Guides expand on these key issues, and can be used as a training tool to emphasize the critical steps relevant to practice in primary care.[1]

99 The faecal specimen. An example where the clinical management of the patient, specimen collection, relevant details on the request form, communication of the result, and public health involvement are all correctly managed. The steps in the process can be divided into seven critical steps (see Chapter 1, 1).

Critical step 1: Collection of a faecal specimen is clearly indicated. With the history, public health should be informed now, and given all necessary details. This gives them the earliest opportunity to investigate a potential outbreak, including retrieval of food samples. The patient should be informed that public health may contact them for further information.

Critical step 2: The patient must be given information on how to collect the specimen.

Critical step 3: The request form details that shellfish were eaten at the reception.

Critical step 5: The faeces bench in the laboratory notes that shellfish were consumed. Selective plates for vibrio are inoculated.

Critical step 6: Salmonella is identified; the laboratory must inform the primary care physician and public health of this result now.

Critical step 7: The patient is contacted by the primary care physician to review his condition, and decide further management as necessary.

The patient is reminded that public health will want to contact him, if not done so already. With the same organism isolated from the patient's faecal specimen and a food type that was consumed, the public health department have the essential information to complete their investigation, which should result in identifying and eliminating any ongoing source of the organism.

Storing and transport of the faecal specimen

Faecal specimens should preferably be delivered to the laboratory within 4 hours of collection. Continued growth of the bowel flora at room temperature lowers the pH in the specimen, which kills bacteria such as shigella (see **123**). If faecal specimens cannot be delivered to the laboratory promptly, they must be refrigerated in the designated refrigerator to arrest the growth of these bacteria. (In order to visualize the trophozoites of *Entamoeba histolytica* and *Giardia lamblia*, a 'hot stool' should be delivered to the laboratory within an hour of it being passed. The laboratory must be informed in advance that such a specimen is being sent; **123**).

99

CRITICAL STEP 1:
Is collection of a specimen indicated?

A 25-year-old male patient presents with a history of profuse diarrhoea of 24 hours duration. Two days before he was at a wedding reception at a hotel, attended by over 100 individuals; he knows that at least 5 others are unwell.

- Assess the patient, give advice on hydration, personal hygiene, and not to return to normal activities until at least 48 hours symptom free.
- Ask the patient details of where the wedding reception took place, confirm the number of people attending, and ask which foods he consumed. Of the three courses served at the reception, the first course was a shellfish pasta.
- Inform the local public health department now.

CRITICAL STEP 2:
Obtain a good quality specimen.

Give the patient advice on how to collect the faecal specimen, and to submit this promptly.

CRITICAL STEP 3:

Record the full patient and clinical details and type of specimen on the request form. Where necessary record the specific test request.

Request form should state summary of clinical details, the relevant history, and details of foods eaten. In this case, shellfish were consumed; this is documented on the request form.

CRITICAL STEP 4:

How is the specimen stored and what is the frequency of transport to the laboratory?

Ensure prompt transport to the laboratory

CRITICAL STEP 5:

What is the quality of the laboratory process, including turnaround times?

The laboratory notes that shellfish were eaten at the reception. Selective agar plates for vibrio are inoculated as well.

CRITICAL STEP 6:

Is immediate or routine reporting of this result required by the laboratory?

Result must be communicated NOW by the microbiologist to the primary care physician and to public health

CRITICAL STEP 7:
How is the laboratory report interpreted?

Report on BA, 25-year-old male:

Cryptosporidium oocysts NOT seen
Campylobacter NOT isolated
E. coli O157 NOT isolated
Salmonella sp. isolated
Shigella NOT isolated
Vibrio parahaemolyticus NOT isolated

The patient is contacted by the primary care physician, to inform him of the result. The patient is much better, but is only 24 hours symptom-free. He must still not resume normal activities. Public health may still visit, if not done so already.

Because of prompt communication at the first visit, public health and the EHD were able to retrieve food for analysis from the hotel kitchen fridge. The Food and Environmental laboratory subsequently report salmonella of same phage type as that from patient being isolated from the hotel's "home-made" mayonnaise.

Quick Action Guide – 1

Managing the patient at the first visit

(Adapted, in part, from *Infectious Diarrhoea; Role of the Microbiological Examination of Faeces; Quick Action Guide for Primary Care* [www.hpa.org.uk]).[1] With permission of the UK Health Protection Agency.)

Patient presents with acute diarrhoea, usually defined as three or more episodes a day, with or without vomiting.

Obtain the full history.

Fill out the request form, and include details of:
- Was there any specific exposure to food or other sources (water, animal) of infection?
- Has there been any recent foreign travel?
- Have shellfish been consumed?
- Has the patient taken any antibiotics recently, either in the hospital or the community? Request CDAD.

Give the patient advice on rehydration and personal hygiene. Does the patient require hospital admission and/or antibiotics?

Give the patient advice on how to collect the specimen, and provide a specimen container.

If working, inform patient they must contact their OHD.

Is this case likely to be part of an outbreak? If YES, inform public health now.

Inform the patient that they must contact the practice/clinic if their condition worsens, or there is no improvement within 48 hours.

If the diarrhoea has stopped, culture is rarely indicated, as recovery of the pathogen is unlikely; exceptions are for specific occupational health or public health requirements; see Appendix.

A stool specimen should be sent:
- Patient is systemically unwell.
- Blood or pus in stool.
- Foreign travel; request OCP.
- Persistent diarrhoea; request OCP for giardia.
- For reassurance, as diagnosis of infection can exclude other diagnoses.
- After antibiotics and hospitalization. (*Clostridium difficile*).

Quick Action Guide – 2

Reviewing the laboratory report, and contacting the patient

Also refer to *Infectious Diarrhoea; Role of the Microbiological Examination of Faeces; Quick Action Guide for Primary Care* (www.hpa.org.uk)[1]

Microbiologist telephones with positive result: *Salmonella* sp. isolated.

- Laboratory should notify the result to the local public health department.
- Contact the patient and review their clinical condition:
  - Improved; can resume normal activities after 48 hours of normal stool.
  - No improvement; consider antibiotics (contact medical microbiologist for advice).
  - Inform patient that public health officers likely to visit to investigate likely source of infection.
  - If there is a duty to do so, notify public health as well.

Final laboratory report received; no pathogen identified.

- Cryptosporidium oocysts NOT seen
  Campylobacter NOT isolated
  E. coli O157 NOT isolated
  Salmonella NOT isolated
  Shigella NOT isolated

  Toxigenic *Clostridium difficile* NOT detected
- Patient not better;
  - Review history and clinical condition. Does the patient need hospital referral?
  - Discuss case with medical microbiologist/infectious disease physician.
  - Consider collecting repeat stool specimen; should OCP be requested?

ORGANISMS AND EPIDEMIOLOGY

About 20% of individuals develop infectious diarrhoea each year.[2–4] In certain parts of the world, children <2 years of age can have six or more episodes/year.[5] Relatively few individuals seek medical help for diarrhoea, and of these only a proportion submit a faecal sample for examination, of which only 2–5% will reveal a pathogen upon laboratory investigation.[3] It is these specimens that provide the key for recognizing and then investigating both local and national outbreaks of gastroenteritis.

100

Diarrhoea in the community

Bacteria:	Campylobacter* Salmonella* Shigella* *Escherichia coli* O157 (HUS, ARF)* *Clostridium difficile* (CDAD)
	Vibrio parahemolyticus (associated with consumption of undercooked shellfish)
Viruses:	Norovirus Rotavirus Adenovirus
Parasites:	Cryptosporidium* *Giardia lamblia* (giardiasis)

'Hospital associated' (especially 60 years)

Bacteria: *Clostridium difficile* (toxin: CDT)

Travel associated

Bacteria:	*Vibrio cholerae* Enterotoxigenic *Escherichia coli* (ETEC)
Parasites:	*Entamoeba histolytica* (amoebiasis) *Giardia lamblia* (giardiasis)

Miscellaneous

Bacteria:	*Yersinia enterocolitica* (mesenteric adenitis, especially children)
	Bacillus cereus, Clostridium perfringens, Staphylococcus aureus (acute toxin-induced food-poisoning)

*In the UK, cryptosporidium, campylobacter, salmonella, shigella, *Escherichia coli* O157, are routinely examined for in all stools; most laboratories will also screen faecal specimens of adults for the toxin of *Clostridium difficile* (CDT).

100 A list of the bacteria, viruses, and protozoa that are associated with diarrhoea and/or vomiting. (HUS: haemolytic uraemic syndrome; ARF: acute renal failure). The acute toxin-inducing bacteria are usually identified in incriminated foods first. See Appendix, Chapter 7 for more detailed information.

Organisms to consider are shown in **100**, and include a range of bacteria, viruses, and protozoa. Laboratories in the UK routinely examine faecal specimens by culture for campylobacter, salmonella, shigella, and *Escherichia coli* O157, and using Ziehl–Neeslen staining, by microscopy for the oocysts of cryptosporidium. The faeces of children under 4 years of age are examined for rotavirus and adenovirus by enzyme immunoassay (EIA) tests. Faecal specimens are routinely examined for the toxin of *Clostridium difficile* (CDT) in patients aged 65 or older; some laboratories will routinely examine the faecal specimens from all adult patients for CDT.

The two important species of the genus *Cryptosporidium* are *Cryptosporidium hominis* and *Cryptosporidium parvum*, the human and bovine genotypes, respectively.[6] Several factors determine the spread of this infection. Oocysts are infectious when they are shed, facilitating easy person-to-person spread. As the infectious dose is very low, and oocysts are very stable, resisting disinfection (including low-level chlorination), long-term, low-grade contamination of recreational waters can occur. *C. parvum* can cause outbreaks in families or groups who visit rural areas where domestic water supplies come from private wells or pumps. These water sources can become contaminated with the

organism that is washed into the ground from the droppings of farm animals. There is also a risk to main water supplies following heavy rainfall if water treatment works do not use filtration, and rely on chlorination alone.

Information on foreign travel should prompt the laboratory to do microscopy for ova, cysts, and parasites (OCP), noting that entamoeba and giardia are not visualized by the stain used for cryptosporidium. Culture plates for *Vibrio cholerae* will also be inoculated as directed by the relevant travel history. Enterotoxigenic *Escherichia coli* is a common cause of traveller's diarrhoea, but is rarely examined for in UK laboratories due to the cost and technical complexities of doing this.

Investigation for other organisms requires specific clinical details to be entered on the request form. This is usually necessary if the pathogen is thought to be relatively uncommon and there is a significant added cost in examining for it. Therefore, such organisms are only examined for when clinical details identify particular risk factors. An example is *Vibrio parahaemolyticus* a cause of gastroenteritis which is invariably associated with shellfish. In order for *Vibrio parahaemolyticus* to be isolated, special selective media need to be inoculated, and key to the laboratory performing this test is the mention of seafood in the clinical details. As a Centres for Disease Control (and Prevention) (CDC) report notes, there are about 4500 cases of *Vibrio parahaemolyticus* infection notified each year in the USA.[7] This is likely to be a significant underestimate, as laboratories are infrequently prompted to use the selective culture media for vibrio, as request forms seldom state that shellfish have been consumed.

As outlined in Chapter 1, norovirus causes infections in the community that probably affect thousands of people during an outbreak. The ease with which norovirus can spread is exemplified by a report where a single worker vomited in a hotel kitchen sink. Despite the sink being cleaned before being used to cool potatoes for a salad, over 50% of 111 guests became ill following a wedding reception held the next day; the potato salad was epidemiologically identified as the source.[8] The virus can have significant economic consequences. *The Times* (London), November 1st 2003, reports on eight outbreaks of norovirus on cruise ships between the period November 2002 to September 2003. In one situation, passengers from a ship were barred by the local authorities in Dubrovnik, Croatia, and Athens, Greece from coming ashore.[9]

Hospitals are the main source of antibiotic-associated diarrhoea (CDAD), caused by the toxin-producing anaerobe, *Clostridium difficile*. With the movement of patients, especially those over 60 years in particular, between the hospital and the community setting, the wide use of antibiotics and the rapid discharge of patients, the recognition of this entity in primary care is important (see Chapter 2). It should be noted that in the community, where CDAD has become more common, in nearly 25% of cases, no traditional risk factors (links to healthcare) are identifiable.[10] This underlines the importance of testing all adult patients with diarrhoea for CDT.

Staphylococcus aureus and *Bacillus cereus* reproduce in food stored at ambient temperature and secrete an emetic, usually heat-stable, toxin, which causes food-poisoning, mainly vomiting, within 1–4 hours of consumption.[11] In the case of *Staphylococcus aureus*, food can be inoculated by a kitchen worker, who is a 'nasal carrier'. *Bacillus cereus* is a sporulating bacterium, and spores can survive the cooking of rice; they then germinate and reproduce in food stored at ambient temperature. *Bacillus cereus* along with *Clostridium perfringens* can also cause later onset disease (8–14 hours), with abdominal cramps and diarrhoea. Here it is *in vivo* production of toxin by the bacteria reproducing in the ileum that causes the disease.[12] Sporadic cases of food poisoning due to the above organisms will not be identified because laboratories do not routinely investigate for such pathogens on individual patients. However, where the laboratory has been informed of an outbreak by public health, samples will be investigated appropriately. To identify these toxin-associated infections, especially in outbreaks, public health and environmental health officers would also obtain samples of the suspected food(s) consumed, which are then examined for these bacteria. As necessary, bacterial isolates are sent to a reference laboratory where strain typing is done. If, for example, an outbreak of food poisoning is associated with one genotype of enterotoxigenic *Staphylococcus aureus*, kitchen workers can be screened for nasal carriage of the organism. If this identifies a carrier, hygiene practices in the kitchen must be improved; nasal decontamination with mupirocin can be considered.

One less common form of food poisoning, termed scrombrotoxin, occurs when fish such as tuna, mackerel, and sardines are stored at room temperature, allowing the normal resident bacteria to multiply, converting histidine in the fish to histamine.[12] Within minutes of consumption, this food can produce an acute histamine reaction, with rash, headache, burning in the mouth, vomiting, and diarrhoea. Histamine is not destroyed by cooking. Histamine levels in food can be measured, confirming again the importance of a food history, and the environmental health department (EHD) obtaining a sample for examination.

Consumption of imported foods is another example of how organisms that cause gastroenteritis impact on public health.

The protozoal parasite cyclospora caused large outbreaks of gastroenteritis in the USA and Canada, with the source being fresh raspberries grown in South America, where they had been contaminated with bird faeces.[13]

Faecal specimens can account for about 10% of the specimens received in the laboratory from primary care. The age and sex distribution of a representative number of patients from whom these were collected is shown in **101**. There are fluctuations in the proportional representation of each age group, depending on such factors as rotavirus activity in children at a particular time of the year. Not surprisingly, and unlike urine specimens, there is little difference between the sexes, as infectious agents causing diarrhoea have no reason to discriminate on the basis of sex. Figures **12–19**, Chapter 1, shows the 'activity' of various pathogens over several years in an area of the UK, based on laboratory confirmed cases. The relative numbers of campylobacter and *Escherichia coli* O157 should be noted.

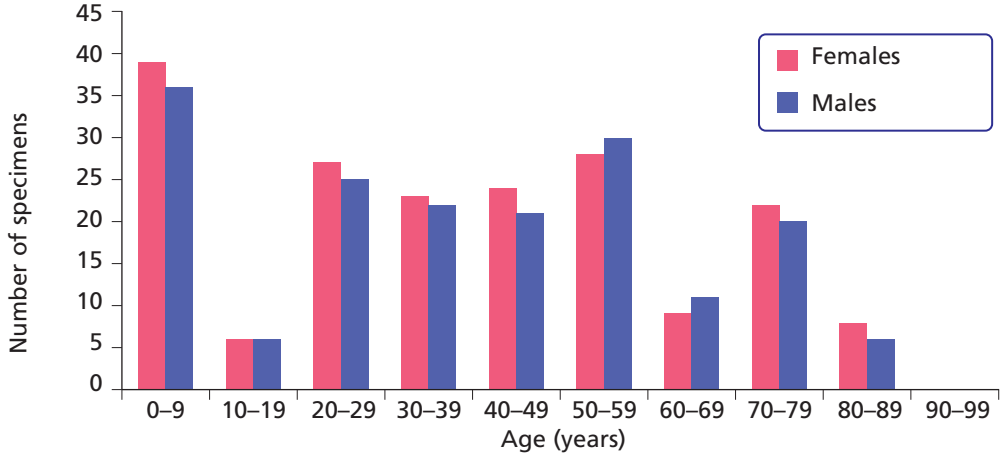
As with most infections, gastroenteritis exhibits a wide spectrum of illness, from those who are asymptomatic, those with abdominal cramps, through to individuals with profuse vomiting and diarrhoea who require hospital admission. When considering all types of infections in the community, infectious diarrhoeal illnesses have an ongoing impact on public health. As discussed in Chapter 1, while outbreaks of gastroenteritis may be restricted to a family, not infrequently they affect the wider community, and outbreaks of food poisoning are regularly reported from social functions such as wedding receptions. A single case of *Escherichia coli* O157 infection in one area may have been acquired elsewhere, such as at an animal 'petting farm' in another county or even country. Each individual case where *Escherichia coli* O157 is identified must prompt a public health investigation as to the likely source.

SPECIFIC ISSUES WITH THE FAECAL SPECIMEN

With reference to the critical steps in **99**, and the Quick Action Guides, the following points should be considered in the patient with infectious diarrhoea:

- The medical management of the patient.
- Advice about personal hygiene, and the need to resume normal activities, which includes work, school attendance, only when at least 48 hours symptom-free.
- Occupational health officers at the place of work or school must be informed by the patient or their carer.
- Giving advice to the patient on safe specimen collection.
- Giving full information on the request form.
- The transport of the specimen to the laboratory.
- Recognizing that the affected individual may be part of an outbreak, and that public health must be informed in such instances.

101



101 The age and sex distribution of the patients from the community who submitted stool specimens to the laboratory over a period of 1 week.

- Once an organism has been identified, the necessary notification to public health. (In the UK this will be done by the local laboratory.)
- Deciding if it is safe for the patient to go back to their normal activities (nursery, school, work, or recreational). This is the role of public health.

A public health problem

As an example of public health implications, consider the real-case situation below.

On weekend duty, the medical microbiologist is reviewing completed microbiology reports prior to authorizing them and notes the results of three faecal specimens, received late 2 days earlier, which had the following details on the request form:

AB, male Age: 20 Address: Sunflower Hall, Training College

Primary care practice/clinic: Evergreen; Dr Brown Date: 10/XX/YY

Clinical details: Diarrhoea +++

Culture: Presumptive salmonella species identified; sent to reference laboratory for confirmation.

BC, male Age: 21 Address: Sunflower Hall, Training College

Primary care practice/clinic: Evergreen; Dr Brown Date: 10/XX/YY

Clinical details: Vomiting and diarrhoea for 3 days.

Culture: Presumptive salmonella species identified; sent to reference laboratory for confirmation.

CD, male Age: 19 Address: Sweet Pea Hall, Training College

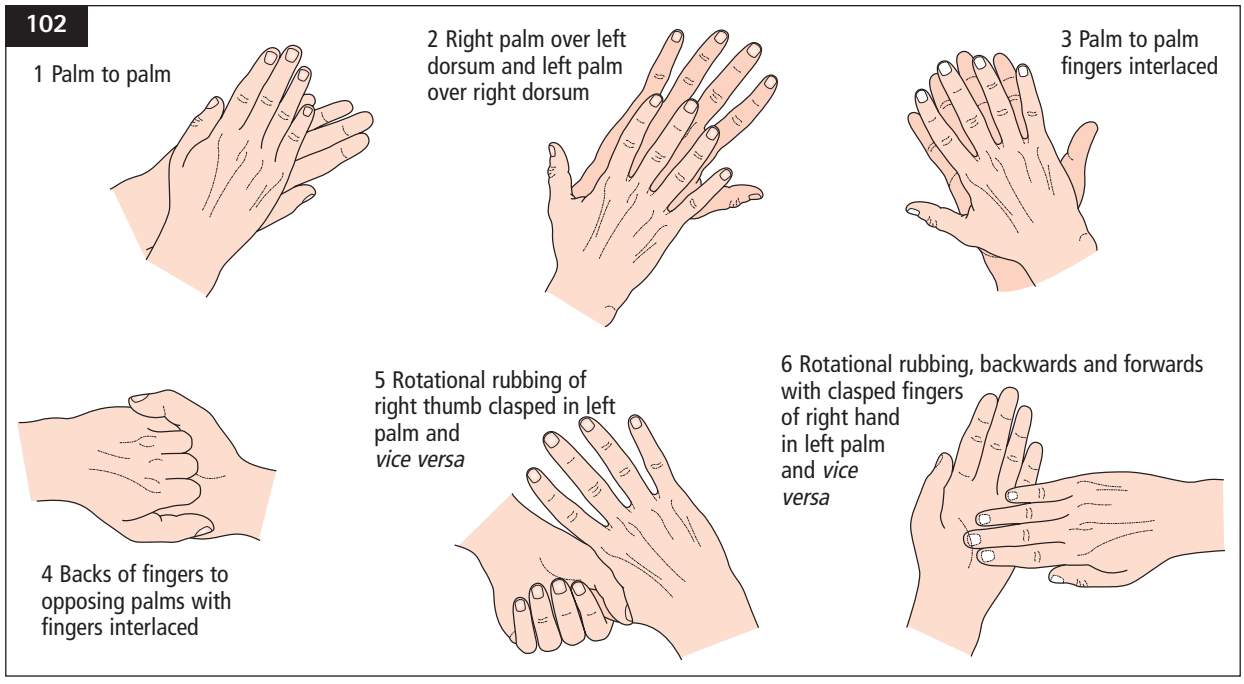
Primary care practice/clinic: Evergreen; Dr Black Date: 10/XX/YY

Clinical details: Recent D&V, faeces still loose

Culture: Presumptive salmonella species identified; sent to reference laboratory for confirmation.

The three samples had been submitted under the name of two primary care practitioners that served the local higher education training college. The medical microbiologist informed the public health doctor on-call that these three cases of likely salmonella gastroenteritis were probably linked by place of abode and/or occupation. Public health then involved the local EHD. Questioning the three students revealed that they had all consumed a 'take-away' from a mobile food-vending facility close to the college, and had developed symptoms later in the week that were sufficiently severe for them to seek medical advice. Further information elicited by the EHD revealed that one item in common consumed was mayonnaise. This was 'homemade' by the vendor using fresh eggs, and was 'topped-up' on a regular basis; a sample of this was collected by the EHO, which grew a strain of salmonella that was identical to that isolated from the three faecal samples. The source of the outbreak was removed, and a successful local authority prosecution was brought against the mobile food vendor. In such a situation, it is frequently unclear how many other individuals had been infected in the past, and over what period of time, as most would not seek medical advice, or then submit a specimen for examination.

There are two important points arising from this incident. The first is that Dr Brown saw two patients from the same college residence, and this should have been an alert to obtain further details, and notify public health immediately of a possible outbreak of food poisoning. Even if Dr Brown had only seen one patient, on relevant enquiry a history of others being affected with similar symptoms may have been elicited, which would have been sufficient to inform public health. Primary care physicians have a key public health role to play here, as they are in the unique position to recognize the situation first. The second point is that the collection of faecal specimens for examination played an essential part in the management of this outbreak. The same organism was isolated from the patients' specimens and the food, enabling the food-poisoning investigation to be completed successfully and the source eliminated.


102
1 Palm to palm
2 Right palm over left dorsum and left palm over right dorsum
3 Palm to palm fingers interlaced
4 Backs of fingers to opposing palms with fingers interlaced
5 Rotational rubbing of right thumb clasped in left palm and *vice versa*
6 Rotational rubbing, backwards and forwards with clasped fingers of right hand in left palm and *vice versa*

102 The Ayliffe hand-washing technique is advisable at all times in the health-care setting. Adequate supplies of disposable hand towels and the appropriate clinical waste bins must always be available. (Reproduced with permission of BMJ Publishing Group.[14])

PRIMARY CARE

The patient with severe gastroenteritis should preferably be seen at home. If they do attend the practice/clinic, they should be seen promptly. Other patients and staff will be at risk if the patient vomits, so the affected individual should wait in a separate area as necessary. In general, adequate facilities for hand washing with pump-action soap dispensers must be available, noting that alcohol hand rub is not active against norovirus and *Clostridium difficile*. Hand washing should be thorough, and the Ayliffe technique practised (**102**).[14]

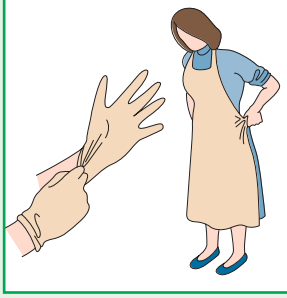
If contamination of the environment occurs with body fluids such as vomit or faeces, thorough cleaning must take place using a disinfectant with appropriate activity, such as freshly made-up hypochlorite solution. An outline of safe disinfection practice is shown in **103**. It can be difficult to remove norovirus from carpets (steam cleaning may work), and these may need to be taken up and destroyed. There is thus good reason for not having carpet in patient areas.

103 Primary care facilities and nursing/residential homes should have clear procedures for dealing with spills of body fluids. A standard operating procedure (SOP) such as that shown together with training should be available as with all the necessary equipment immediately. (Note that for blood spills, available chlorine has to be 10 000 ppm; a separate SOP should be available for this.) Bottles should be clearly labelled and fresh solutions made up daily, and the date recorded on the bottle.

103

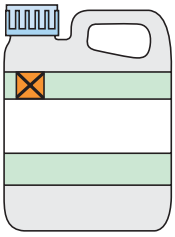
For Terminal Cleans, Isolation Cleans, Outbreak Cleans, etc.

NOT SUITABLE FOR USE ON BLOOD SPILLS – SEE BLOOD SPILL POLICY



Always wear protective gloves and an apron.

Ensure good ventilation

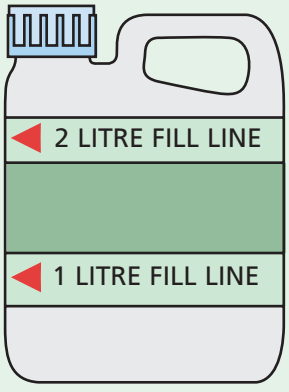


Refer to CoSHH note on product label and check expiry date.

Use 2 tablets for 2 litres of cold water

= 1 000 p.p.m. Available Chlorine

Use 1 tablet for 1 litre of cold water



Use with disposable cloths or mops to wipe over surfaces or floors.

Discard any remaining solution.

Dos and Don'ts

- ✔ **Make a fresh solution each day or shift.**
- ✔ Store in accordance with the CoSHH regulations.
- ✔ Change solution when it becomes dirty.
- ✘ Don't shake the container to mix
- ✘ Don't use directly on urine or vomit
- ✘ **NEVER** mix with any other cleaning agent or any chemical.
- ✘ **Never use in a spray bottle.**
- ✘ Never make up with hot water

THE PATIENT

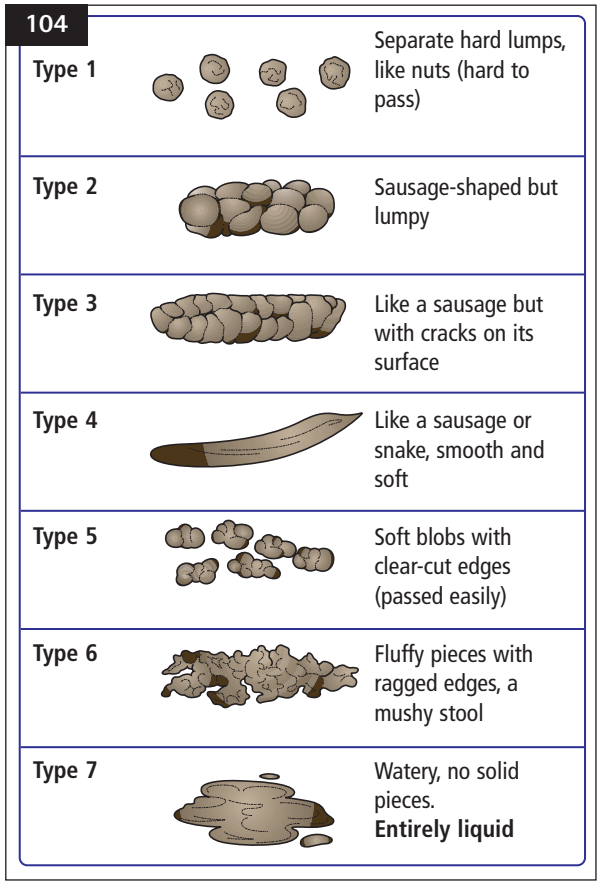
Patients who present with 'the runs' usually have significant diarrhoea and should be asked to submit a faecal sample for examination. They often blame a particular meal especially if it was not cooked at home, but not infrequently the time scale of events does not fit this association. A food history over the past 72 hours should be taken. Further questioning can determine that there may have been a lapse in hygiene in the home. When managing patients in a care or nursing home, it is useful to use the Bristol stool chart (**104**).[15] This chart enables comparative assessment of the faeces of individual patients to be scored on an ongoing basis, and a record should be kept to monitor this over the duration of the illness.

Although serious illness occurs at the extremes of age, gastroenteritis can be extremely disabling for the healthy adult as well, who may require hospital admission. However, the majority of cases are self-limiting and oral rehydration will suffice. Once vomiting has begun to settle, and fluids can be taken, oral rehydration salts (ORS) are suitable for children; one option for adults is a soft drink such as 'flat' cola.

In relation to public health, most patients can be advised to resume normal activities only after they have been symptom-free for 48 hours. However, certain individuals/occupations are considered to have an additional risk, and these are listed in **105** and may need to be managed on advice of public and/or occupational health.[16]

Recurrent or prolonged infection with the same organism should be an alert to other conditions. For example on-going salmonella infection should be an alert for an HIV test, as this condition is more common in HIV-infected patients. Chronic diarrhoea is defined as longer than 14 days' duration, and when examination of faecal specimens for 'routine organisms' is negative, other causes must be considered.[17] HIV infection is again a consideration. Causes of chronic diarrhoea are shown in **106**.

104


Type 1
Separate hard lumps, like nuts (hard to pass)
Type 2
Sausage-shaped but lumpy
Type 3
Like a sausage but with cracks on its surface
Type 4
Like a sausage or snake, smooth and soft
Type 5
Soft blobs with clear-cut edges (passed easily)
Type 6
Fluffy pieces with ragged edges, a mushy stool
Type 7
Watery, no solid pieces.
Entirely liquid

104 The Bristol stool chart, based on the original article by Lewis and Heaton (1997).[15] This chart is useful for 'scoring' each motion produced by the patient, and is of particular relevance in managing the patient with CDAD, and the response to treatment. A score of 5–7 is regarded as being consistent with diarrhoea. (Reproduced with the permission of Dr KW Heaton.)

105

A: Any person of doubtful personal hygiene or with unsatisfactory toilet, hand-washing or hand-drying facilities at home, school or work.

B: Children who attend pre-school groups or nurseries.

C: People whose work involves preparing or serving unwrapped foods not subjected to further heating.

D: Clinical and social care staff in high-risk facilities who have direct contact with susceptible patients, or people in whom gastrointestinal infection would have particularly serious consequences.

In general individuals **NOT** in categories A–D are excluded from their normal activities until 48 hours after the person is free from diarrhoea and/or vomiting. If there is any doubt, the local public health department should be contacted, who will determine when it is appropriate for individuals to return to school or work. Occupational health departments should also be informed of every individual who is away from work with diarrhoea.

105 For public health purposes, individuals falling in the categories A–D are considered an increased risk in the spread of organisms transmitted via food or the faecal–oral route. See the Appendix for further details on specific organisms. The occupational health departments should be informed.

106

Infectious conditions to consider, if not fully excluded:

- Has the laboratory investigated for all the appropriate organisms? This is dependent on clinical information, i.e. travel abroad for vibrios, aeromonas and parasites. For parasites, where excretion is intermittent, at least three stool samples should be submitted on alternate days.
- Giardia. This can be difficult to diagnose microbiologically (see **123**).
- Amoebiasis. (See **123**.)
- Has a specimen been examined for *Clostridium difficile* and CDT?
- Cryptosporidiosis. Chronic infection/diarrhoea can indicate underlying immunosuppression.
- HIV; it is always worthwhile to consider an HIV test in the patient with chronic diarrhoea.
- CMV colitis in the patient on immunosuppressive therapy (and the HIV-infected patient). Consider contacting the medical microbiologist/infectious diseases physician.

Noninfectious conditions:

- Bowel malignancy.
- Bowel surgery.
- Carbohydrate malabsorption.
- Crohn's disease.
- Endocrine disorders (adrenal, diabetes, thyroid).
- Inflammatory bowel disease.
- Lactose intolerance in children.
- Ulcerative colitis.

- Alcohol.
- Antiarrhythmic agents.
- Antihypertensive agents.
- Caffeine.
- Laxative abuse, including 'dried' prunes.
- Sucrose/fructose 'abuse'; excessive consumption of sweeteners, confectionary, and dried fruit, e.g. prunes.

106 When diarrhoea persists for more than 14 days, it should be considered chronic and further investigation is required.

COLLECTING THE SPECIMEN

All cases of diarrhoea should be regarded as infectious unless evidence indicates otherwise. Patients should be advised about the appropriate precautions, and methods of collecting a faecal specimen. Passing the specimen directly into the specimen pot is not practical and simple steps can be taken in the home to pass the faeces into a more suitable receptacle first, followed by transfer to the specimen pot (**107–123**). A specimen from a child may be collected from a nappy, or even collected off the floor, before this is carefully cleaned. Waste should be responsibly disposed of through the domestic system; soiled plastic containers should be 'double bagged', and placed promptly in the outside household bin. Finally, the patient or carer, must clean and dry their hands scrupulously after these procedures.

After collection, the specimen should be transported to the laboratory as soon as possible, as the faecal microenvironment changes with time, exemplified by a falling pH. This reduces the likelihood of organisms surviving until the faeces is processed in the laboratory; shigella is particularly labile.[18] To minimize these changes, faecal specimens should be refrigerated in a designated refrigerator if there is a delay in transport. Key points to bear in mind with the collection of faecal specimens are shown in **123**, page 123.

THE REQUEST FORM

Laboratories analyse faecal specimens for a set of common pathogens. However, additional clinical details will alert the laboratory to investigate a wider range of pathogens. The relevant box in Quick Action Guide 1 should be referred to.

THE LABORATORY REPORT

The laboratory will usually inform the practice/clinic by telephone when an organism is identified, and also inform public health. At this stage it is important to contact the patient (see Quick Action Guide 2):

- To discuss the result with the patient, and its implications.
- To determine if they have improved or not. Most individuals will have improved and can return to normal activities after being symptom-free for 48 hours. If the patient falls into special risk groups then further review will be required either by public health or occupational health before they return to their normal activities (**105**).
- If the patient has not improved, treatment needs to be reviewed; antibiotics are occasionally indicated and this should be discussed with the infectious disease physician or medical microbiologist. Does the patient require referral to hospital?
- To inform the patient in advance that they will be contacted by the public health department for further information on the likely source of the infection.

The report issued by the laboratory is usually straightforward, stating that none of the pathogens are present, or that a named pathogen has been identified. On occasion, several bacterial pathogens and parasites may be identified in a single faecal specimen! Certain organisms such salmonella and *Escherichia coli* O157 are sent to the UK National Reference Laboratory for confirmation of their identity, typing, and where relevant, toxin production (e.g. *Escherichia coli* O157; verotoxin-producing organism). The first report may state 'Presumptive *Salmonella typhimurium* isolated; sent to reference laboratory for confirmation'.

When confirmation of the identity and strain typing is returned from the reference laboratory, a second report should be issued with this information. Typing is an essential tool for public health purposes; several isolates of an unusual serotype of salmonella for example, from different parts of a country, may be the first indication of a wider/national 'outbreak' by that particular strain.

Occasionally, the reference laboratory report reveals that the submitted organism is in fact not a pathogen. This occurs because some nonpathogenic bacteria may occasionally be misidentified as a pathogen by the local laboratory being closely related biochemically and antigenically, for example, to shigella. When the primary care physician is told that the initial positive result has been amended by the local laboratory, this can be exasperating, as information given to the patient or their family, and to public health, has to be withdrawn. However, it is important to recognize that for a number of bacteria, a 'presumptive' identification has to be used and the reference laboratory confirmation awaited. From a practical perspective, for public safety reasons, the initial result must be acted upon.

107

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111

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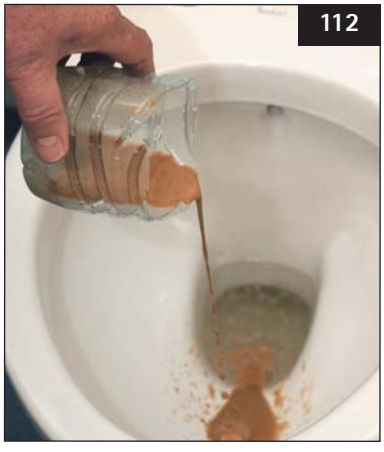
110


112

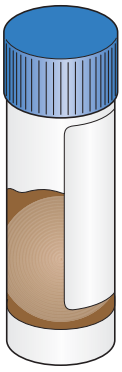
113

114

107–114 Advice for the adult in the collection of a stool specimen. All the necessary items should be in place first. **(107, 108)** An empty water bottle can be cut with kitchen scissors and used as the receptacle. **(109)** The patient should ensure that details of their name, date of birth, time and date of collection are recorded on the specimen container. **(110–112)**. The specimen is collected, and poured carefully into the specimen container, no more than one-third full. The lid must be *firmly* applied; the remainder of the specimen is carefully discarded into the toilet. **(113)** The empty receptacle is 'double-bagged' in two disposable plastic bags, and disposed in the outside council household refuse bin. **(114)** Hands must be washed well with soap and warm running water; the underneath of nails should be carefully cleaned as well. It is after this that underwear, trousers, and belt should be fastened.

115–122 Collecting a stool specimen from a child; roles of the parent/carer. (**115–117**) Preparation should be done first, with labelling of the specimen pot, removal of watch and jewellery, and, if possible, the use of disposable household gloves. (**118–120**). The sample can be collected from a cleaned potty that is free of detergent. A nappy or specimen on the floor can also be collected, but are of poorer quality, especially if contaminated with urine. (**121**) Any spills must be collected with toilet tissue, and well cleaned with household detergent. The potty must be thoroughly cleaned. Used gloves should be 'double bagged' in two disposable plastic bags, and disposed in the outside council household refuse bin. (**122**) Hands must be thoroughly washed with soap and hot water, including under the finger nails. They *must* be rewashed before any food preparation.

123



Submit to the laboratory, preferably within 4 hours of collection. If this cannot be done, store in a **designated** practice/clinic refrigerator.

Rectal swabs are a poor substitute for a stool specimen.

The specimen pot should be labelled with the name and date of birth of the patient. Ensure all the relevant clinical, travel, and exposure details are included on the request form, in order to assist the laboratory.

Specimens should be collected in a wide-mouthed receptacle, and then transferred to the specimen pot (see **107–122**).

Liquid (diarrhoea) stools should be sent to the laboratory; solid specimens are of little use, and should not be submitted, unless there is a specific public health reason (see Appendix). The container should not be filled to more than 1/3, and the lid firmly screwed down.

Specimens contaminated with urine are of poor quality. Residual detergents used to clean potties can inactivate pathogens.

Organisms such as shigella die as the pH falls. If transport is delayed, the specimen can be kept overnight in the designated refrigerator that is NOT used for storing food or drugs.

SPECIMEN COLLECTION FOR SPECIFIC ORGANISMS

Amoebiasis (*Entamoeba histolytica*)

A stool sample is the usual specimen.

In order to find trophozoites, a fresh stool specimen must be examined within 1 hour of collection. It is important to contact the medical microbiologist to coordinate the receipt and examination of such specimens.

Giardiasis (*Giardia lamblia*)

In order to find trophozoites, a fresh faecal specimen must be examined with 4 hours of collection. Because of the intermittent nature of cyst shedding, it may be necessary to examine three or more samples collected on alternate days to exclude this infection. It is important to contact the medical microbiologist to coordinate the receipt and examination of such specimens.

Enterobiasis (threadworm or pinworm)

Faecal specimens have a low sensitivity.

A swab should be moistened in sterile saline and repeatedly rolled over the whole perianal area. The swab is then cut off into a white-topped specimen container with a few mL of sterile saline.

Female threadworms lay eggs onto the perineum during the night, and thus the optimum sampling time is on waking, and before showering or defaecation. If appropriate, a parent or carer can collect a swab as outlined above. The rest of the swab and packet contents can be disposed of in household waste. Household scissors used to cut the swab should be carefully cleaned, and hands well washed afterwards.

Repeated sampling over 4–6 days may be needed to exclude the diagnosis.

EGGS ARE HIGHLY INFECTIOUS, AND RESIST DRYING. HANDS AND SCISSORS MUST BE SCRUPULOUSLY DISINFECTED AFTER SAMPLING.

123 The blue-topped stool container should be used for transporting the specimen to the laboratory. Some important points about specimen collection for specific organisms are listed.

124

Organism	Antibiotics (oral adult doses)
Campylobacter	Antibiotic therapy usually has little effect on duration of symptoms, unless given very early in the illness course, but this criterion is seldom met. In the minority who have ongoing diarrhoea clarithromycin 500 mg q12h for 5–7 days can be given; advice can be sought from the medical microbiologist/infectious diseases physician.
Clostridium difficile	Metronidazole 400 mg q8h for 14 days; if symptoms do not settle within 4–6 days, seek advice from the medical microbiologist/infectious diseases physician. For relapses, as second-line treatment, vancomycin, 125 mg q6h by mouth is given for 14 days.
Salmonella (non-enteric fever)	Usually not given; seek advice from the medical microbiologist/infectious diseases physician for severe/persistent diarrhoea. In immunocompromised patients (including HIV infected) diarrhoea may be unduly severe, and there is a risk of bacteraemia. Ciprofloxacin 500 mg q12h for 7 days or azithromycin 500 mg q24h for 5 days. Co-trimoxazole and amoxicillin can be alternative treatment options.
Shigella dysenteriae	Choice of agent based on antibiotic susceptibility profile. Ciprofloxacin 500 mg q12h for 3 days, or azithromycin 500 mg q24h for 3 days can be given. Seek advice from the medical microbiologist/infectious diseases physician.
Shigella other than *dysenteriae*	Antibiotics are helpful, and can be life-saving. Seek advice from the medical microbiologist/infectious diseases physician especially for severe/persistent diarrhoea. Options include ciprofloxacin 500 mg q12h for 3 days, or levofloxacin 500 mg q24h for 3 days, or azithromycin 500 mg q24h for 3 days.
Entamoeba histolytica	Metronidazole 800 mg q8h for 5 days (if only intestinal disease) followed by either diloxanide furoate 500 mg q8h for 10 days, OR paromomycin 25–35 mg/kg/day in three divided doses for 7 days to eliminate luminal cysts. For extraintestinal infection seek advice from the medical microbiologist/infectious diseases physician.
Giardia lamblia	Metronidazole 400 mg q8h for 5 days or metronidazole 2 g daily for 3 days.
Cryptosporidium	Usually self-limiting in immunocompetent individuals. Various agents including paromomycin, trimethoprim-sulfamethoxazole, nitazoxanide, and azithromycin have been used, but success is variable. In the immunocompromised, restoration of immune function is important. Expert advice should be sought from an infectious diseases or STD physician.

124 Fluids are the mainstay of treatment. Antibiotics that can be used to treat infectious gastroenteritis are listed (adult doses). Antibiotics should not be given for suspected or confirmed infection due to *Escherichia coli* O157. The risk of CDAD due to *Clostridium difficile* should be considered with antibiotic treatment.

TREATMENT

Fluid replacement is the mainstay of treatment (see previous section). While specific antimicrobial therapy is used for treating *Shigella dysenteriae*, *Clostridium difficile*, giardiasis, and amoebiasis, antibiotics are generally withheld for other organisms.[12] However, particularly severe or protracted diarrhoea with campylobacter, salmonella, or *Shigella* non-*dysenteriae* may require antibiotic treatment (**124**). Antibiotics are currently contraindicated with *Escherichia coli* O157, as they

may increase the release of the toxin.[19] The patient with bloody diarrhoea should be an alert. Haemorrhagic colitis, haemolytic uraemic syndrome (HUS), and acute renal failure (ARF) are life-threatening complications of *Escherichia coli* O157, and the young and old are particularly susceptible. Antimotility agents should not be used when there is fever, or blood in faeces, signs that would indicate invasive disease, or when CDAD is suspected.[20]

With *Entamoeba histolytica* and *Giardia lamblia*, metronidazole is the mainstay of treatment.[21] For amoebiasis, cyst carriage should be eliminated by the use of diloxanide furoate or paromomycin.[21] There is really no consistent and reliable antibiotic treatment for cryptosporidium.[6] Most infections are self-limiting, but in AIDS patients and other immunocompromised individuals, life-threatening or protracted infection can occur. However, the restoration of immunity by the use of antiviral agents enables the HIV-infected individual to control this infection.[22]

CLOSTRIDIUM DIFFICILE AND CDAD

This section is included here to highlight some key points in the diagnosis and treatment of CDAD, summarised in **125**. As stated in Chapter 2, CDAD is a recognised entity in the community, and should be considered in all adult patients with diarrhoea who have recently had antibiotics, particularly those considered to be of higher risk such as the fluorinated quinolones and cephalosporins. It should be noted that CDAD is also identified in patients who have no clear risk.[10] Because it is a potentially life-threatening infection, especially in the older debilitated individual, every effort should be made to confirm the diagnosis so that the patient can be appropriately managed. For this reason many laboratories in the United Kingdom will screen unformed faecal specimens from all adult patients for CDT.

Clostridium difficile secretes two protein toxins, A and B, that cause the disease. In order to detect toxin producing organisms, laboratories can use one or more of number of tests. These include tissue culture and a cytotoxicity assay, an EIA for both toxin proteins, and a PCR molecular test for the toxin gene(s). In order to screen faecal specimens first for the presence of the organism, an EIA that detects the *Clostridium difficile* specific glutamate dehydrogenase enzyme (GDH) is often used. GDH is a good marker for the presence of *Clostridium difficile* in faeces, as it is produced in high concentrations (constitutively) by all strains of the organism, irrespective of whether they are toxin producers or not.[23] The GDH test is sensitive and specific, with a negative predictive value of over 99%. A positive result confirms the presence of the organism, while a negative results indicates that it is absent.[23, 24] In many laboratories, current practice is to test GDH-positive faecal specimens for the toxin gene(s) by PCR (**125** *overleaf*). The combination of the GDH screening test, followed by the molecular test has a high sensitivity and specificity, and is an acceptable cost-effect two-stage process.

While it will not be practical with the individual patient at home, staff in nursing and care homes should keep a record of bowel motions of each affected patient, using the Bristol Stool Chart. With this information, it is essential to assess the patient clinically and to determine if they have mild, moderate, or severe disease. This classification is very important, and patients who have moderate disease should also be assessed for the need to refer them to hospital. It should be noted that peripheral white cell count (WCC), renal function, and C-reactive protein (CRP) are useful markers to monitor outcome. It is certainly reasonable to have baseline values for these tests for patients with moderate disease at least.

HYGIENE PRACTICES

The information below is taken, in part, from the report of the Working Group of the Former PHLS Advisory Committee on Gastrointestinal Infections.[16]

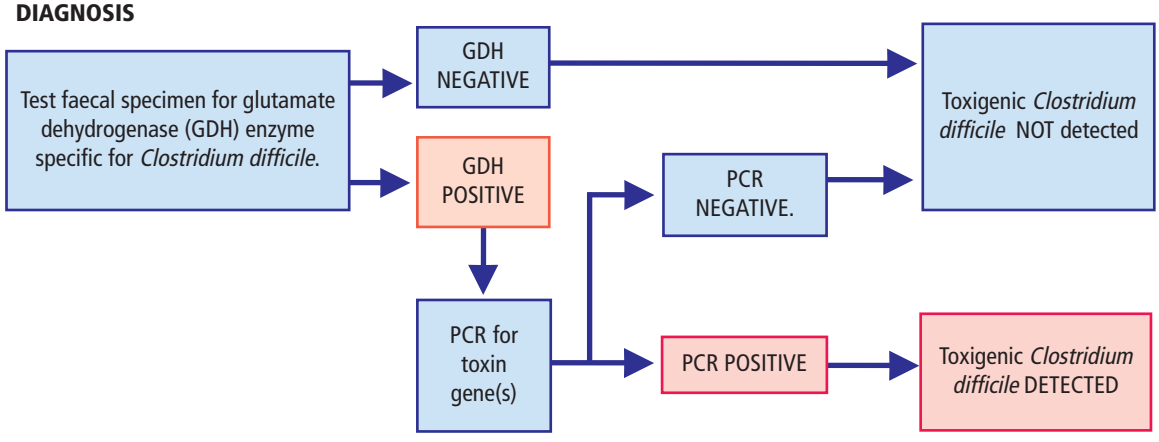
The home environment

The mainstay of infection control in gastroenteritis is enteric precautions, consisting of hand washing, disposal of secretions and spillages, and decontamination. If a home has an additional separate toilet this should be designated for the single use of the affected person for the duration of the illness. Hands must be washed immediately after defaecating, underwear, pants, and belt should be adjusted, before washing hands again. This prevents contamination of the belt buckle in particular.

Enteric precautions and a high standard of personal hygiene should always be emphasized with the patient. In the private home, unless essential, the ill individual should not prepare food until at least 48 hours after their first formed faeces. Prevention measures in the home include advice on not preparing raw meat and uncooked food such as salads on the same board, table, or with the same utensils. It is also wise to prepare salads before handling potentially contaminated food, such as raw chicken. Hands must be frequently washed with soap and water. Care must be taken when storing food such as salad in the same fridge as uncooked meat, to ensure cross-contamination does not occur.[16]

125

DIAGNOSIS


Test faecal specimen for glutamate dehydrogenase (GDH) enzyme specific for *Clostridium difficile*.
GDH NEGATIVE
GDH POSITIVE
PCR for toxin gene(s)
PCR NEGATIVE.
PCR POSITIVE
Toxigenic *Clostridium difficile* NOT detected
Toxigenic *Clostridium difficile* DETECTED

MANAGEMENT

'Mild' disease; <4 motions/day (type 5, 6, or 7) on Bristol stool chart, peripheral WCC normal:

- Stop precipitating antibiotics where possible. Avoid anti-motility agents.
- Monitor fluid intake and electrolytes.
- No specific treatment may be needed.
- If treatment given, metronidazole 400 mg q8h for 14 days.

'Moderate' disease; 3–5 motions/day (type 5, 6, or 7) on Bristol stool chart, peripheral WCC 10-15 x 10^9/L:

- General measures as above. Consider hospital referral.
- Metronidazole 400 mg q8h for 14 days.
  If no response in 48 hours, consider replacing metronidazole with vancomycin 125. mg q6h for 14 days and consider seeking urgent advice.*/**

'Severe' disease; >4 motions/day (type 5, 6, or 7) on Bristol stool chart, fever >38.5ºC, dehydration, abdominal distension, and peripheral WCC > 15 x 10^9/L:

- Conduct immediate referral to hospital NOW.**
- Give first dose of metronidazole NOW.

* Contact the medical microbiologist.
** Contact the infectious diseases physician.

PRACTICE POINTS

Inform the patient (or their carer):

- To always inform all HCW, as necessary, about the diagnosis of *Clostridium difficile* infection.
- To seek medical advice if symptoms have not resolved within 4 days of starting treatment, or symptoms are still present on completion of treatment.
- To seek immediate medical advice if symptoms return following completion of treatment. (Note that there is a 20-30% relapse rate).

If the patient has developed infection in any communal setting (i.e. nursing/residential home), inform public health as there can be a risk of further cases, or the patient may be part of an undiagnosed outbreak.

The work environment

The symptomatic individual, who handles food in the community, should not come to work. If symptoms develop at work they must stop work immediately, and report this to their immediate manager (it might be decided to discard food they have been involved with and to clean toilet facilities) and the occupational health officer. In schools and institutions especially, adequate hand-washing facilities must be available. The toilet hygiene of young children, those with learning difficulties, and the elderly, should be closely supervised. The specific risk groups cited in **105** should be referred to.[16]

Hand washing

Thorough hand washing with soap in warm running tap water is very important. Doctors, nurses, relatives, and other carers must wash their hands before and after contact with patients. Hands must also be washed after handling soiled clothing, bedding, equipment, and after removing disposable gloves. Everyone, including the patient, must wash their hands after defaecating, or having changed the nappy/diaper of a baby. Hands must always be washed before preparing, serving, or eating food. Cleaning under nails is important and towels must not be shared. In primary care settings and in institutions, pump-action liquid soap dispensers and disposable hand towels should be used; alcohol hand-rub dispensers should also be available, and regularly checked to ensure that they are operational. It is important to note that alcohol-based preparations are not active against the spores of *Clostridium difficile*, cryptosporidium, and norovirus; hand washing with soap and water is the mainstay here.

Disposal of excretion and soiled materials

At home, sick people would normally use a flush toilet, and as stated before, a separate toilet, if available, should be designated for use by the affected individual only. Carers, preferably wearing a disposable apron and gloves should empty a bedpan or commode into the toilet, and wash it carefully with hot water and detergent, rinse, and allow to dry. Gloves and aproon should be removed, and the hands washed thoroughly under warm soapy water. Soiled clothing and bed linen should be washed separately from other clothes in a domestic washing machine, using the 'hot' cycle. Obvious faecal material can be scraped off the clothes into a toilet bowel before placing them in the washing machine. Thorough hand washing should be practised, and the outside of the washing machine can be cleaned with hot soapy water after loading.

Spillages and decontamination

All toilet areas and hand basins must be cleaned thoroughly at least once a day.

Spills of faeces, vomit, or urine should be cleaned promptly. The carer should preferably wear disposable apron and gloves. Domestic absorbent kitchen paper towel can be applied first to soak up the fluid and then placed in the toilet. The area should be thoroughly cleaned with water and freshly made solutions of hypochlorite. The toilet bowl, sink, taps, and handles should all be thoroughly cleaned. Disposable gloves and aprons can be 'double bagged' in plastic bags, and disposed of in the domestic waste. Soiled items must not be cleaned in a kitchen sink.

Environmental contamination occurs, and norovirus, rotavirus, and *Clostridium difficile* highlight the need for high hygiene standards in the

125 An outline of the diagnosis and management of *Clostridium difficile* infection. In addition to a full blood count, it is important to do "baseline" tests for renal function and C-reactive protein, as these are also useful markers to monitor outcome.
The GDH enzyme specific for *Clostridium difficile* is produced by both toxigenic and non-toxigenic strains, and an EIA for this enzyme is used as the screening test. (A negative GDH test has a high negative predictive value for excluding *Clostridium difficile*). If the faecal specimen is GDH-positive, a second test for the toxins is done. One methodology is a molecular test detecting the presence of the toxin gene(s). If the specimen is found to be positive for the toxin gene(s), a report is issued stating 'toxigenic *Clostridium difficile* DETECTED'. If the molecular test is negative for the toxin gene(s), the report will state 'toxigenic *Clostridium difficile* NOT detected'. The reason for two-stage testing is mainly driven by cost. Samples could be tested by the molecular method alone but the cost would be prohibitive in many situations.

community. Norovirus is present in vomit and faeces; aerosolized vomit contaminates surfaces and uncovered food. All food, wrapped or unwrapped should be discarded, as it is impossible to clean the outside of such items. All surfaces must be carefully cleaned with a chlorine-based detergent, and washing down with copious amounts of fresh water afterwards. Typical of clostridia, *Clostridium difficile* survives in the environment as heat-stable spores. In the nursing home, where there is a cohort of potentially susceptible patients, all surfaces should be kept clean; inspections of the underside of commodes and surfaces of bed-pans should be done to ensure cleaning has been adequate. Protocols for safe cleaning in nursing homes should be available (**103**, page 117).

When referring a patient with suspected infective gastroenteritis to hospital, it is essential to warn both the ambulance service (if used) and the admissions unit of the hospital of the likely infective nature so they can take precautions from the outset to minimize spread.

SUMMARY AND KEY POINTS

In summary, the following points should be noted:

- The practice/clinic should establish guidelines for clinical and nursing staff to use so that there are set criteria, centred on the Quick Action Guides and the critical steps of **99**.
- These should be used regularly as a training tool to give guidance on when and how to collect specimens, their storage and transport.
- It is important to follow-up the patient with CDAD during the treatment period of 14 days to ensure that there is improvement. If there is no improvement, advice must be sought promptly from the microbiologist/infectious diseases physician.
- The patient who has been successfully treated for CDAD in the community must be told to contact the practice/clinic promptly if there is a recurrence of diarrhoea.
- Patients who are, or who have been treated for CDAD should be told to inform staff at any other health-care centre they may attend of their *Clostridium difficile* status.
- Primary care physicians are in a unique position to identify outbreaks of food poisoning in the community. A careful history which elicits this information is so important, so that public health can be informed at the earliest opportunity.

A summary of the organisms considered in this chapter is given in the Appendix. This is based on the comprehensive publication by the Working Group of the former PHLS Advisory Committee on Gastrointestinal Infections.[16] This is included as general information for the primary care physician.

8

The Eye and the Respiratory Tract Specimen

- Overview
- Introduction
- The eye
- The ear, nose, and throat
- The lower respiratory tract
- Tuberculosis
- Summary and key points

OVERVIEW

In the UK, patients with respiratory tract infections (RTI) account for over 40% of antibiotic prescriptions in primary care.[1] However, these patients generate a small percentage of specimens submitted to the laboratory. Certain organisms such as *Streptococcus pneumoniae* and *Haemophilus influenzae* are recognized as common bacterial pathogens and can cause disease in sites such as the eye, middle ear, and lung, enabling antibiotic guidelines to specify a fairly narrow range of agents to use in empirical treatment. Key to treatment is the use of established guidelines that provide logical steps that determine the need for antibiotics, including 'no antibiotic', 'delayed antibiotic', or 'immediate antibiotic' prescription regimes.[2] Added to this is a flow diagram that can be used in assessing the adult patient with community-acquired pneumonia (CAP), including use of the CRB-65 score to decide whether or not the patient requires hospital admission. If this is the case, immediate administration of an antibiotic should be considered.[3,4]

The main learning points of this chapter are:

- The use of guidelines to assess each patient, and when to consider empirical antibiotic prescription. In general, microbiology specimens for the culture of bacteria are infrequently helpful in management of acute RTI.
- When samples are submitted, recognition that there are potential pitfalls from collection through to interpretation of the result.
- That culture of sputum is primarily of value in patients with chronic lung disease (cystic fibrosis, chronic obstructive pulmonary disease [COPD], bronchiectasis), or where pulmonary tuberculosis (TB) is suspected.
- When pulmonary TB is suspected, three early-morning sputum samples, collected on consecutive days, must be sent to the laboratory, with the request form detailing 'acid fast bacilli (AFB) microscopy and culture'. If a sputum is 'smear positive' for AFB, the patient should be referred immediately to a TB specialist. Even if microscopy for AFB is negative on the three specimens, referral must still be done if TB is still strongly suspected clinically.
- That nucleic acid amplification test (NAAT) such as polymerase chain reaction (PCR) are now available for diagnosis of a range of pathogens, including influenza, parainfluenza, respiratory syncitial virus (RSV), metapneumovirus, and mycoplasma. The availability, and funding, for these tests should be confirmed locally.

INTRODUCTION

The discrepancy between the frequency of antibiotic prescription and paucity of microbiology specimens submitted is due to a number of factors. These are that many upper RTIs are viral in origin, the difficulty of obtaining sputum samples in patients with acute pneumonia (and the low diagnostic yield), and the usual predictability of the most common bacterial pathogens, and their antibiotic sensitivities.[2–5] However, it is important to submit a specimen in particular circumstances, including the patient not responding to empirical treatment and is now producing sputum, those with chronic lung disease, and where pulmonary TB is suspected. The scenario in **126** highlights a case where the primary care physician had not considered the possibility of TB in this individual because, although unwell with a chronic cough, the patient was young, well-nourished, employed, and was not identified as being in a potential risk group. It should be noted that a RTI is not infrequently an alert for underlying human immunodeficiency virus (HIV) disease. If this infection is confirmed, it widens the range of organisms to consider, for example *Pneumocystis jirovecii*, which will directly alter the management of the patient.

126

CRITICAL STEP 1:
Is collection of a specimen indicated?

A 19-year-old female patient has a productive cough of 5 weeks duration. Courses of amoxicillin, co-amoxiclav, and erythromycin have been given.

CRITICAL STEP 2:
Obtain a good quality specimen.

No respiratory pathogens have been identified in two specimens. The latest recent report states: 'Profuse growth of coliforms'.

CRITICAL STEP 3:

Record the full patient details and type of specimen on the request form. Where necessary, record the specific test request.

CRITICAL STEP 4:

How is the specimen stored and what is the frequency of transport to the laboratory?

CRITICAL STEP 5:

What is the quality of the laboratory process, including turnaround times?

CRITICAL STEP 6:

Is immediate or routine reporting of this result required by the laboratory?

CRITICAL STEP 7:
How is the laboratory report interpreted?

The primary care physician phones the medical microbiologist to ask for the antibiotic susceptibility profile of the 'coliforms'. The relevance of this is discussed.

In view of chronic nature of the infection, the microbiologist recommends examination of sputum samples for mycobacteria.

All three sputum samples contain profuse alcohol acid-fast bacilli, subsequently confirmed as *Mycobacterium tuberculosis*. The patient is promptly referred to the respiratory physician and public health are notified.

126 The sputum specimen. An example where a wider range of organisms has not been considered in the patient with a cough of 5 weeks' duration. The steps in the process can be divided into seven critical steps (see Chapter 1, 1).

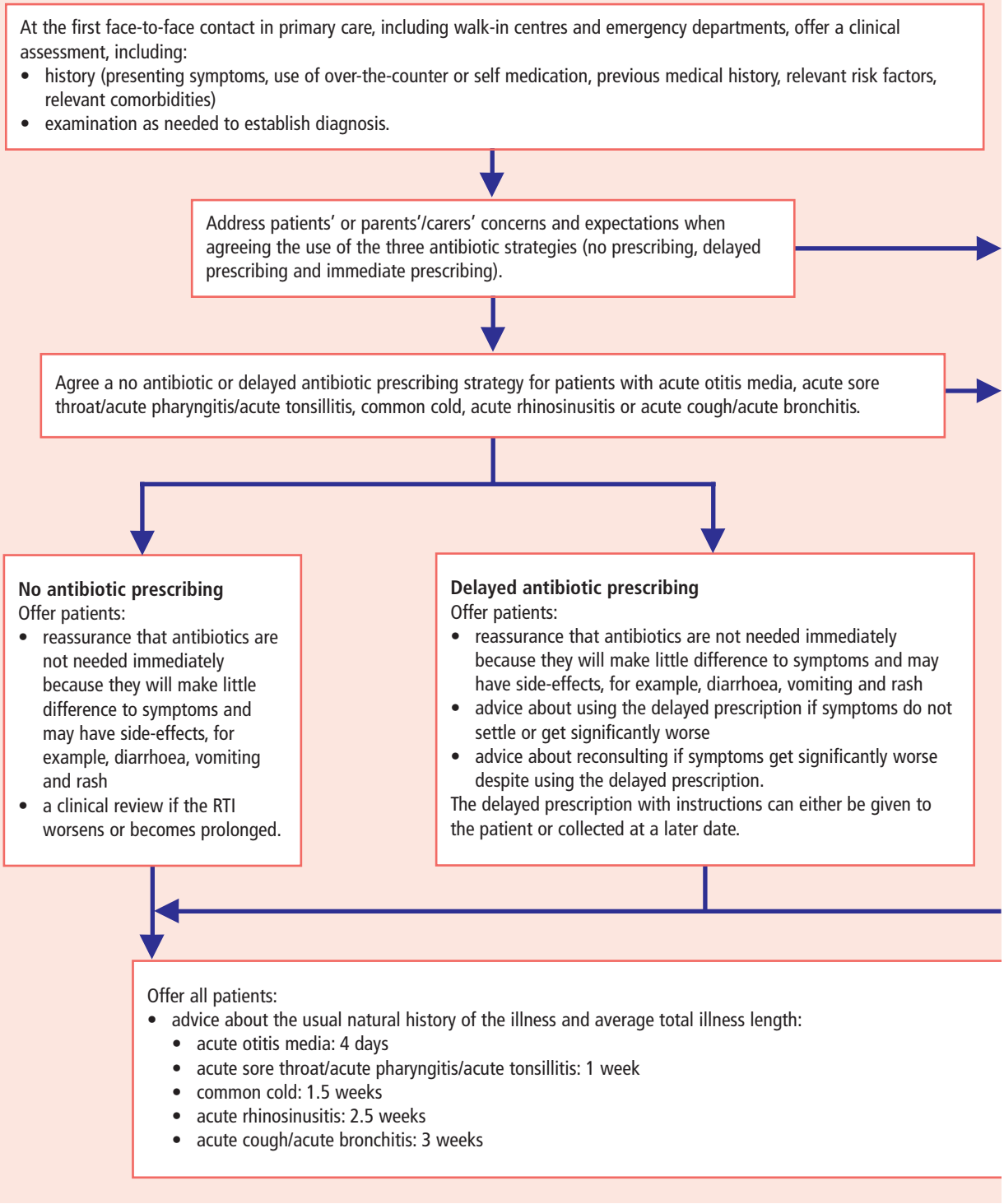
In this scenario, three sputum samples had been collected, two earlier in the illness, from which no respiratory pathogens were identified, and the latest, taken after 5 weeks into the illness which grows a profuse growth of 'coliforms'. The 'coliforms' are likely to be due to their overgrowth in the oropharynx, being selected out by antibiotics. The lack of antibiotic sensitivity information is now fortuitous, prompting the primary care physician to consult the medical microbiologist, when the likelihood of tuberculosis (TB) is raised. This had not been considered before, as the patient was considered to have no risk factors for TB, being young, employed, previously fit and well, and from an ethnic group with a low incidence of the disease. This case emphasizes consideration of a wider range of organisms in all patients with a chronic cough, including TB. An HIV test is negative.

Storing and transport of the sputum specimen

Instructions must be given about sputum collection, and the patient should be told that saliva is not the appropriate sample. Where possible, sputum should be obtained in the early morning, when pooled secretions after sleep are available. Brushing teeth and rinsing well with water (not proprietary mouthwash or gargles which may contain antibacterial substances) has been shown to reduce the number of contaminating oropharyngeal bacteria. Specimens are collected into the usual container for sputum. In order to minimize contaminating the outside of the container, the patient should be advised to place the rim of the container to the lower lip, and cough the expectorate into the container. Specimens should be transported to the laboratory as soon as possible, or stored in the designated refrigerator if there is a delay, in order to arrest growth of oropharyngeal contaminants (e.g. 'coliforms').

Quick Action Guide

Care pathway for respiratory tract infections (RTIs). National Institute for Health and Clinical Excellence (2008). Adapted from CG 69 Respiratory tract infections: antibiotic prescribing. NICE, London. Available from www.nice.org.uk/CG69. Reproduced with permission.[2]


At the first face-to-face contact in primary care, including walk-in centres and emergency departments, offer a clinical assessment, including:
• history (presenting symptoms, use of over-the-counter or self medication, previous medical history, relevant risk factors, relevant comorbidities)
• examination as needed to establish diagnosis.
Address patients' or parents'/carers' concerns and expectations when agreeing the use of the three antibiotic strategies (no prescribing, delayed prescribing and immediate prescribing).
Agree a no antibiotic or delayed antibiotic prescribing strategy for patients with acute otitis media, acute sore throat/acute pharyngitis/acute tonsillitis, common cold, acute rhinosinusitis or acute cough/acute bronchitis.
No antibiotic prescribing
Offer patients:
• reassurance that antibiotics are not needed immediately because they will make little difference to symptoms and may have side-effects, for example, diarrhoea, vomiting and rash
• a clinical review if the RTI worsens or becomes prolonged.
Delayed antibiotic prescribing
Offer patients:
• reassurance that antibiotics are not needed immediately because they will make little difference to symptoms and may have side-effects, for example, diarrhoea, vomiting and rash
• advice about using the delayed prescription if symptoms do not settle or get significantly worse
• advice about reconsulting if symptoms get significantly worse despite using the delayed prescription.
The delayed prescription with instructions can either be given to the patient or collected at a later date.
Offer all patients:
• advice about the usual natural history of the illness and average total illness length:
• acute otitis media: 4 days
• acute sore throat/acute pharyngitis/acute tonsillitis: 1 week
• common cold: 1.5 weeks
• acute rhinosinusitis: 2.5 weeks
• acute cough/acute bronchitis: 3 weeks

Quick Action Guide

The patient is at risk of developing complications.

Immediate antibiotic prescribing or further investigation and/or management
Offer immediate antibiotics or further investigation/management for patients who:

- are systemically very unwell
- have symptoms and signs suggestive of serious illness and/or complications (particularly pneumonia, mastoiditis, peritonsillar abscess, peritonsillar cellulitis, intraorbital or intracranial complications)
- are at high risk of serious complications because of pre-existing comorbidity. This includes patients with significant heart, lung, renal, liver or neuromuscular disease, immunosuppression, cystic fibrosis, and young children who were born prematurely
- are older than 65 years with acute cough and two or more of the following, or older than 80 years with acute cough and one or more of the following:
  - hospitalization in previous year
  - type 1 or type 2 diabetes
  - history of congestive heart failure
  - current use of oral glucocorticoids.

However, also consider an immediate prescribing strategy for the following subgroups, depending on the severity of the RTI.

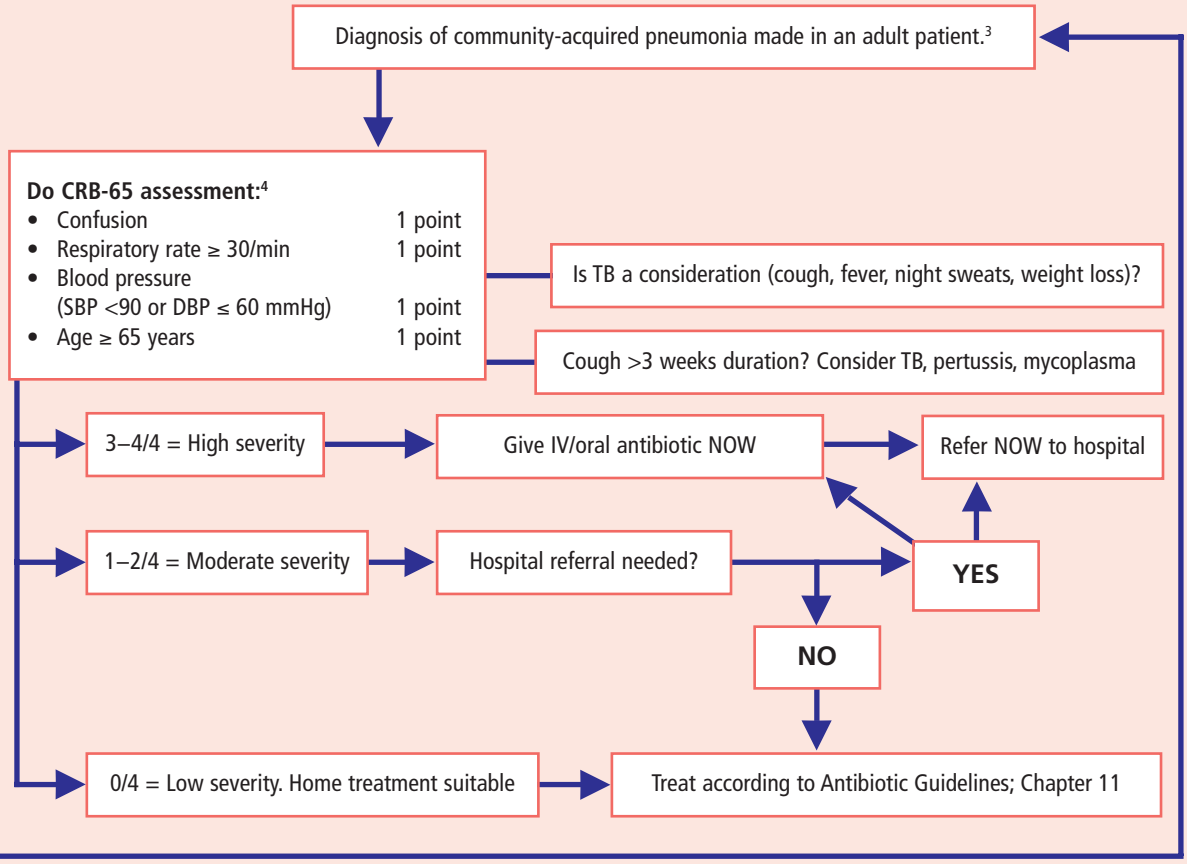
Immediate antibiotic prescribing
Depending on clinical assessment of severity, also consider an immediate prescribing strategy for:

- children younger than 2 years with bilateral acute otitis media
- children with otorrhoea who have acute otitis media
- patients with acute sore throat/acute pharyngitis/acute tonsillitis when three or more Centor criteria are present.*

*Centor criteria: presence of tonsillar exudate, tender anterior cervical lymphadenopathy or lymphadenitis, history of fever, and absence of cough

- advice about managing symptoms including fever (particularly analgesics and antipyretics). For information about fever in children younger than 5 years, refer to '*Feverish Illness in Children*' (NICE Clinical Guideline 47).

Quick Action Guide



With urgent referral to hospital for community-acquired pneumonia the following antibiotics should be given at the practice/clinic or home:

If no history of penicillin allergy: Benzylpenicillin IV, or IM if a vein cannot be accessed, 1200 mg, or amoxicillin 1 g by mouth.

If penicillin cannot be given (e.g. due to allergy to penicillin): Consider cefotaxime or ceftriaxone IV, or IM if a vein cannot be accessed, 1 g.

With azithromycin 500 mg or moxifloxacin 400 mg ONCE

(For patients having home treatment it is reasonable to give the first dose of the antibiotic in the Practice)

Infections of the eye, ear, and respiratory system as a whole are caused by endogenous or exogenous organisms. *Streptococcus pneumoniae* is a minor member of the normal flora of the nasal epithelium. When the function of the cilia of the eustachian tube is compromised by a viral infection, pneumococcus can ascend to initiate otitis media. Pneumococcus can enter the bronchial tree by microaspiration of oropharyngeal fluid during sleep (a natural phenomenon distinct from gross aspiration). If the ciliated respiratory epithelium is compromised, sufficient numbers of pneumococci (low numbers of a virulent strain may be sufficient) can reach the lungs to initiate pneumonia; the otherwise healthy smoker is more at risk of pneumococcal pneumonia because of the toxic effect of smoke on the function of this ciliated epithelium.[6]

Exogenous organisms usually reach the respiratory tract in some form of droplet. Influenza virus is expelled from the respiratory tract of an infected individual within large droplets. These rapidly fall out of the air by gravity and do not travel further than 1–2 metres. Individuals may become directly infected if the droplets impact on the mucosa of the mouth or eye. The virus can also survive on surfaces from where it can be introduced into the nose or mouth by fingers which have touched a contaminated surface. Reproducing in the nasal epithelium, influenza can then spread to the throat, trachea, bronchi, and lungs. Legionella and TB are examples of true air-borne spread of infection. These organisms can remain suspended in the air for prolonged periods of time. Infection occurs when susceptible individuals breath in the organisms which then reach the lungs directly.

127

Staphylococcus aureus (MSSA and MRSA)
Group A streptococcus
Streptococcus pneumoniae

Haemophilus influenzae
Moraxella catarrhalis

Neisseria meningitidis
Neisseria gonorrhoeae (neonatal conjunctivitis)

Pseudomonas aeruginosa (important in wearers of contact lenses)

Chlamydia trachomatis

Adenovirus
Coxsackie virus

HSV1
VZV

Acanthamoeba (important in wearers of contact lenses)

127 A list of some important organisms associated with conjunctivitis and/or keratitis.

THE EYE

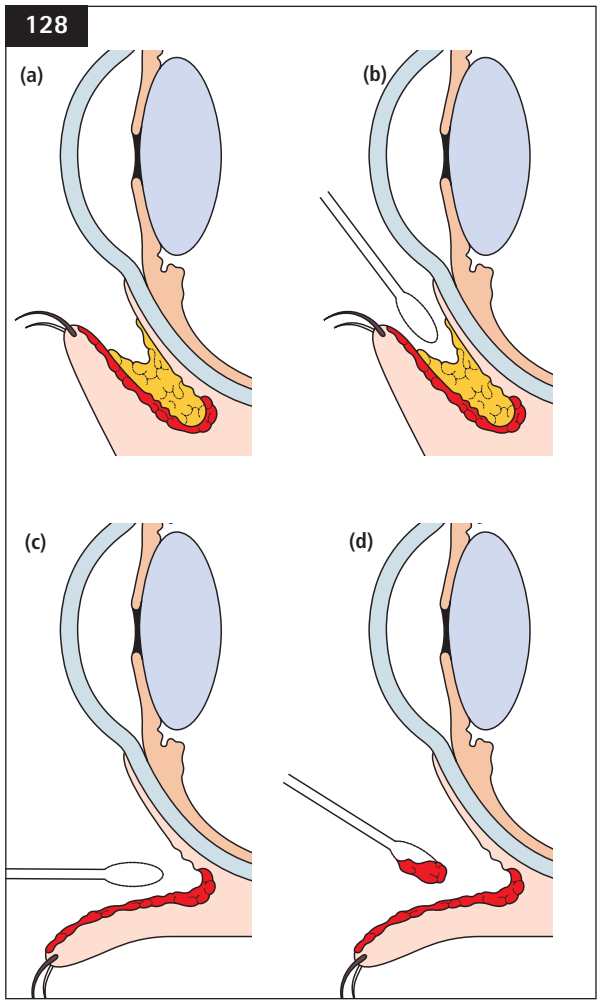
A list of organisms causing infections in the eye is given in **127**. Viral conjunctivitis is characterized by hyperaemia, a watery discharge, and initially starts in one eye and then spreads to the other. Bacterial conjunctivitis is associated with a mucopurulent discharge.[7]

Particular attention should be given to individuals who wear contact lenses. In addition to *Pseudomonas aeruginosa*, acanthamoeba, a free-living protozoa in natural water, is an important cause of keratitis in healthy people, the majority of whom wear contact lenses. Lenses are contaminated when homemade cleaning solutions are used, or swimming or showering with lenses in place.[8] This infection should be considered in any contact lens wearer who has a foreign body sensation, photophobia, and tearing; immediate referral to the ophthalmologist is required.

Chlamydia conjunctivitis is often initially missed in the newborn. It can arise 14 days or so after birth. Prescription of chloramphenicol eye drops temporarily improves the condition, but relapse occurs when the eye drops are stopped, leading to further repeat courses of topical antibiotics before the diagnosis is entertained. When the diagnosis is made, both parents should be treated and investigated for sexually transmitted infection (STI). Being a STI, chlamydia should be considered in all sexually active adults presenting with conjunctivitis, and positive patients, together with their partners, should be treated and investigated for other STI.

Although uncommon, gonococcoccal conjunctivitis can arise promptly after birth, characterized by abrupt onset, and rapid progression to a copious purulent discharge, which rapidly accumulates after being wiped away. Prompt referral to the paediatrician is required.

The patient
With eye infections, the primary care physician will usually diagnose and treat uncomplicated infection in a 'red eye', but eye pain, any visual deficit, or evidence of corneal infiltrate or hypopyon requires immediate intervention by the ophthalmologist. The primary care physician must not simply recommend that the patient seeks help, but must transfer the care of the patient immediately to the ophthalmologist.[7]



128 (**a**) When a specimen is collected, the lower eyelid should be everted to expose the fluid, so that this can be swabbed (**b**). For chlamydia, any discharge should be carefully removed with a swab or sterile gauze to expose the palpebral conjunctiva (**c**). The swab should be carefully rubbed on the conjunctival surface to collect cells containing the intracellular chlamydia (**d**).

Specimen collection
The method of specimen collection in the setting of conjunctivitis is shown in **128**. For chlamydia, the lower eyelid must be fully everted, and any pus removed using a standard 'transport' swab, which can be submitted for bacterial culture. The chlamydia PCR swab should then be rubbed carefully on the conjunctival surface to ensure that cells containing these intracellular bacteria are collected.

The laboratory report
The results need to be reviewed with the likely clinical diagnosis. 'Coliforms' are likely to be of dubious clinical significance, and rarely require treatment.

Treatment
With the exception of chlamydia infections (see below), topical antibiotics are given for conjunctivitis in primary care, but evidence for their effectiveness is mixed. One useful option is to consider delayed antibiotic prescribing, with the self-limiting nature of the condition being explained to the patient, or parents, and a prescription written that can be collected 3 days later if there is no improvement. The use of delayed prescription is associated with reduced antibiotic use, and a similar clinical course when compared to individuals who are given the antibiotic immediately.[9]

Chlamydia infections require systemic antibiotic therapy as the infection is not limited to the eye but can involve the lungs (neonates) and the genital tract. Systemic antibiotics are sufficient and there is no need for topical eye drops to treat the eye infection caused by chlamydia.

THE EAR, NOSE, AND THROAT
A list of organisms causing infection in the middle, external ear, and throat is shown in **129**.

Otitis media
The bacteria usually involved here are pneumococcus, haemophilus, moraxella, and group A streptococci. In most circumstances, specimens are not collected in primary care because of the predictable occurrence of the organisms involved, and unless there is a perforated eardrum discharging pus, there is no specimen to collect.

Otitis externa
Acute localized folliculitis can be caused by *Staphylococcus aureus*, and cellulitis by group A streptococcus; diagnosis and treatment can be straightforward. Diffuse otitis externa is a condition that can be associated with 'swimmer's ear', where bacteria, commonly pseudomonas, grow in the damp and macerated debris in the canal. The

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	Otitis Externa	Otitis Media	Pharyngitis
Staphylococcus aureus (MSSA)	✔✔	✔	
Staphylococcus aureus (MRSA)	✔✔	✔	
Streptococcus pneumoniae		✔✔✔	
Group A streptococcus	✔✔	✔✔	✔✔✔
Group C streptococcus			✔✔
Group G streptococcus			✔
Haemophilus influenzae		✔✔✔	
Moraxella catarrhalis		✔✔	
Neisseria gonorrhoeae			(✔)*
'Coliforms'	✔		
Pseudomonas aeruginosa	✔✔✔**		
Aspergillus niger	✔✔		
Mycoplasma pneumoniae		✔	✔
Chlamydophila pneumoniae		✔	✔✔
Coronavirus			✔
CMV			✔
EBV			✔✔✔
HIV			✔
Influenza virus A and B		✔	✔✔
Parainfluenza viruses		✔	✔✔
HSV			✔✔✔

*Gonococcal throat carriage is usually asymptomatic.
**In addition to diffuse otitis externa, *Pseudomonas aeruginosa* is the causative agent of malignant otitis externa, usually affecting the older diabetic or imunocompromised patient.

129 A list of organisms associated with infections of the ear and throat.

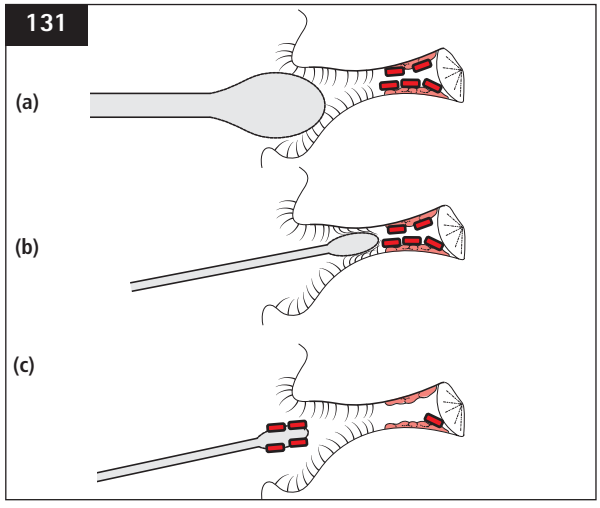
inflammatory response to the bacteria and bacterial products can give rise to significant pain because of the limited space for expansion of the skin and subcutaneous tissue in the external canal. While some ear, nose, and throat (ENT) specialists would treat with aural toilet and anti-inflammatory drops, not infrequently in primary care, repeat courses of topical or systemic antibiotics are given. This leads to overgrowth of 'coliforms', whose relevance is doubtful. The mould *Aspergillus niger* is also associated with diffuse otitis externa. It is of use to note that acetic acid in alcohol preparations can be effective, as they create an acidic environment in which pseudomonas and aspergillus cannot grow.

Malignant otitis externa usually occurs in the older diabetic, or immunocompromised patient; this condition is a medical emergency. *Pseudomonas aeruginosa* is the causative agent, and unlike diffuse otitis externa the infection erodes into the surrounding tissues, including bone and may produce a facial nerve palsy. It is important to differentiate this potentially life-threatening condition from diffuse otitis externa. Significant pain and any evidence of facial nerve palsy warrants immediate referral to the ENT surgeon. Management consists of serial imaging together with a prolonged course of antibiotics, usually a parenteral antipseudomonal antibiotic for several

weeks, followed by oral ciprofloxacin for a further 4 weeks. This is one situation where the benefit of oral ciprofloxacin is considered with the risk of CDAD. On discharge from hospital, the patient should be instructed to contact their primary care physician promptly if diarrhoea develops, so that CDAD can be tested for.

The patient

Patients presenting with infection of the ear and upper respiratory tract should be reviewed with the NICE *Guideline 69 Respiratory Tract Infections* (Quick Action Guide).[2]



131, 131 The 'standard' transport swab is too wide to enter the external ear canal, and the appropriate 'ear' swab should be used to sample the relevant organism. This is shown diagrammatically in diagrams **131a–c**.

Specimen collection

The ear swab

Where specimen collection is indicated, the ENT swab should be used. Standard transport swabs are usually too large to enter the canal, whereas the ENT swab enables deeper sampling to be done, which is more likely to collect the relevant pathogen(s) (**130, 131**). In the setting of a ruptured ear drum and chronic otitis media, discharge blocking the external meatus can be carefully removed with a swab, and a sample collected from the more medial aspect of the ear canal.

The nose swab

Nose swabs are usually collected to detect *Staphylococcus aureus* either because the patient is suffering from recurrent boils/folliculitis or for infection control management when methicillin-resistant *Staphylococcus aureus* (MRSA) screening is required. A standard 'transport' swab should be moistened in sterile saline and passed about 2 cm into the nostril, and rubbed on the wall of both nostrils for 4–5 seconds. Clear details of the test required should be clearly recorded on the request form; for MRSA screening, selective media are used, and routine microscopy, culture, and sensitivity (MC&S) will not be done on the specimen.

The throat swab

Most acute sore throats are viral in origin. Swabbing may occasionally be helpful when the diagnosis is not clear, or there is failure to respond to treatment in the setting of a penicillin allergy, where information on macrolide resistance would be helpful in management. With recurrent pharyngitis, a standard swab can be used to collect pus from the tonsillar area. Other organisms such as Epstein–Barr virus (EBV) need to be considered and the appropriate blood and serology tests done. Remember the HIV test.

The laboratory report

The report should be reviewed to consider the clinical relevance of particular organisms at each site, along with any serology tests that have been done.

The ear swab

The results need to be reviewed with the likely clinical diagnosis. 'Coliforms' are usually of dubious significance, and rarely require treatment. Pseudomonas in the older diabetic or immunocompromised patient should warrant consideration of malignant otitis externa.

The throat swab

Group A, C, and G streptococci are recognized causes of bacterial pharyngitis, whereas group B

streptococci is not. The presence of small numbers of candida may only reflect its position as part of the normal flora. Diphtheria is uncommon and most laboratories no longer routinely culture for this organism. When suspected clinically, the patient should be referred immediately to an infectious diseases physician.

Treatment

The ear

Folliculitis or cellulitis/erysipelas of the ear can be treated with either flucloxacillin or clarithromycin. 'Aural toilet' should be used first to manage diffuse otitis externa, and gentle syringing by an experienced operator with warm 3% saline is one option. This can be followed by clioqinol-flumetasone or betnesol drops containing betamethasone. The patient should lie with one ear up, the drops applied by a carer, and then stay in this position for at least 10 minutes in order to maximize contact with the skin of the affected external ear. An alternative is a solution of 2% acetic acid in 70% ethanol; Earcalm® is an acetic acid spray that can be obtained from the pharmacist for this purpose. Aspergillus may also colonize moist debris in the external ear, and is likely to overgrow following the application of topical antibacterials. Acetic acid also creates an unfavourable environment for aspergillus. Malignant otitis externa requires immediate referral to the ENT specialist.

The nose

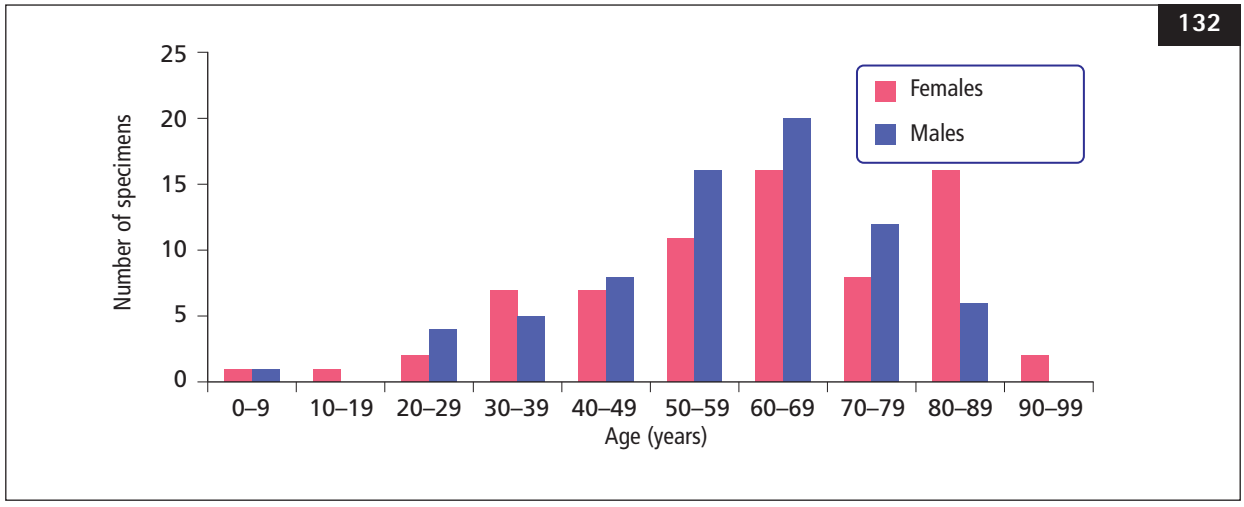
With recurrent boils in the anterior nose, topical mupirocin can be applied to both nostrils three times a day for 5–7 days. On occasion, a systemic antibiotic may be required.

The throat

Streptococcal pharyngitis should be treated with penicillin V or macrolide. For the patient with recurrent infection caused by *Streptococcus pyogenes*, often a young adult, and in whom EBV has been excluded, amoxicillin with oral rifampicin for 7 days can be considered. One reason for recurrent infection is likely to be due to persistence of intracellular streptococci, which are killed by rifampicin. A macrolide can be used in combination with rifampicin in the penicillin-allergic patient, where the organism is sensitive to erythromycin. The interaction of rifampicin with the oral contraceptive should be taken into account.

THE LOWER RESPIRATORY TRACT

The age and sex distribution of patients submitting sputum specimens to the laboratory over a period of a week is shown in **132**. Not surprisingly, patients are mainly in the age group of 50 years plus, and reasons entered on the request form include bronchitis, chronic bronchitis, COPD, and exacerbations of COPD. Overall there is not a significant difference on the basis of sex.



132 The age and sex distribution of the patients from the community who submitted sputum specimens to the laboratory over a period of 1 week.

While infections are often acute, or exacerbations of a condition such as COPD, it is important to consider the organisms involved in chronic infections. Lingering tracheobronchitis/bronchitis and/or cough of >3 weeks duration in the previous healthy individual should prompt consideration of *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, and *Bordetella pertussis*. *Mycobacterium tuberculosis* must be considered at this stage.

Atypical pneumonia is defined as a respiratory infection that begins as a mild RTI, which is followed by pneumonia with dyspnoea and cough without sputum. This definition is now regarded as dated from a clinical perspective, but it identifies a particular group of organisms.[5] In general, the organisms responsible for atypical pneumonia do not grow on laboratory media and traditionally require serology in order to make the diagnosis. However, the more recently introduced PCR tests have revolutionized the diagnosis of these agents. Travel or occupation may expose the individual to legionella in the water system of hotels or commercial properties. While the association between legionella and holidaying abroad is well recognized, most cases of legionella are in fact sporadic and not associated with travel. Perversely, the greatest risk arising out of a holiday may be from the patient's own home, as there will be no turnover of water for some days, favouring the growth of legionella. Of note are reports of Legionnaires' disease in gardeners using potting compost, where the identical strain of *Legionella longbeachae* was isolated from patients and compost used. [10, 11]

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	Pneumonia	Tracheobronchitis	AECB*	COPD*	Cystic Fibrosis**
Staphylococcus aureus (MSSA)	✔✔				✔✔
Staphylococcus aureus (MRSA)	✔✔				✔✔
Streptococcus pneumoniae	✔✔✔		✔✔✔	✔✔✔	
Haemophilus influenzae	✔✔✔		✔✔✔	✔✔	✔✔
Moraxella catarrhalis	✔✔		✔✔✔	✔✔	
Klebsiella pneumoniae	✔				
*Mycobacterium tuberculosis****	✔✔✔				
Pseudomonas aeruginosa				✔✔	✔✔✔
Bordetella pertussis		✔✔			
*Chlamydophila pneumoniae*****	✔✔✔	✔✔✔		✔✔	
*Legionella pneumophila*****	✔✔✔				
*Mycoplasma pneumoniae*****	✔✔	✔✔✔		✔✔	
Coronavirus*****	✔✔	✔✔✔	✔✔	✔✔	
Influenza virus A and B*****	✔✔	✔✔✔	✔✔	✔✔	
Parainfluenza viruses*****	✔✔	✔✔✔	✔✔	✔✔	
RSV*****	✔✔	✔✔✔	✔✔	✔✔	
Pneumocystis jirovecii†	✔✔				

*AECB: acute exacerbation of chronic bronchitis; COPD: chronic obstructive pulmonary disease.

***Burkholderia cepacia* is an important organism in this condition; for infection control purposes, infected cystic fibrosis (CF) patients must not have contact with uninfected CF patients.

***Atypical mycobacteria are also identified on occasion. These include *Mycobacterium avium-intracellulare* (an AIDS-defining illness) and *Mycobacterium kansasii*, *Mycobacterium malmoense*, which can cause infection in previously damaged lungs.

****In addition to *Chlamydophila psittaci* and *Coxiella burnetii*, these are organisms to consider in atypical pneumonia, characterized by dyspnoea, cough, and minimal sputum production.

†Usually considered when the patient is referred to hospital, but it is an important entity to consider in all immunocompromised individuals.

133 Organisms associated with infections of the lower respiratory tract.

A list of important organisms that cause infections of the lower respiratory tract is shown in **133**. Further detailed lists can be found elsewhere.[12–14]

Pneumocystis is likely to be dormant and present in very low numbers in the lungs of all individuals, but takes advantage of the immunosuppressed individual. In HIV infection, the presentation is often insidious with temperature and increasing shortness of breath over many days or weeks. Pneumocystis must be also be considered in other immunosuppressed patients with an unresolving pneumonia, for example, those on high-dose steroids or agents such as azothioprine and methotrexate.

The patient

Patients with pneumonia should be reviewed using the CRB-65 criteria (C: Confusion; R: Respiratory rate; B: Blood pressure; Age ≥65 years). While those with a score of 1 or more are referred to hospital, patients with a score of 0 can be managed in the community.[2, 3] They must be given antibiotics and be reviewed within 48 hours. Many patients do not produce sputum in the acute phase of a lower RTI and microbiological investigation is often not performed.[2]

Collecting the specimen

The decision to collect a sputum sample should be based on the following considerations:

- The lung is not an exocrine gland and the patient with acute pneumonia will often not produce sputum, especially in the first few days of the infection. When a sputum is submitted to the laboratory, there is usually a low diagnostic yield.
- Sputum collection is indicated when the patient shows no response after 48 hours of treatment. However, failure to respond may be due to a variety of reasons and care must be taken in interpreting a sputum culture result taken when a patient is already on antibiotics. A report stating 'Profuse growth of coliforms' usually reflects an overgrowth of the normal flora in the oropharynx by these 'coliforms', which have been 'selected out' by antibiotic use.
- With infection in the setting of chronic lung conditions such as COPD, cystic fibrosis, or bronchiectasis, sputum microbiology is an essential part in management, especially in patients with moderate to severe disease. Sputum is usually readily produced, and as a greater range of bacteria play a role, their highly variable antibiotic susceptibility profiles, arising from significant antibiotic use over the course of the illness, should be known in order to direct treatment. In cystic fibrosis, in addition to *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Haemophilus influenzae*, and *Burkholderia cepacia* are important. Selective media are used to separate out these bacteria from each other. Providing clinical details of the condition is important in ensuring the laboratory performs the appropriate tests.
- When pulmonary TB is suspected (see below).

How to collect the specimen

Instructions must be given about sputum collection, and the patient should be told that saliva in not the appropriate sample. Where possible, sputum should be obtained in the early morning, when pooled secretions after sleep are available (**134**). Brushing teeth and rinsing well with water (not proprietary mouthwash or gargles which may contain antibacterial substances) has been shown to reduce the number of contaminating oropharyngeal bacteria.[15] Specimens are collected into the usual container for sputum (**134**). In order to minimize contaminating the outside of the container, the patient should be advised to place the rim of the container to the lower lip, and cough the expectorate into the container.[16] Specimens should be transported to the laboratory as soon as possible, or stored in the designated practice/clinic refrigerator if there is a delay, in order to arrest growth of oropharyngeal contaminants (e.g. 'coliforms').

134 Collection of the sputum specimen. A salivary specimen (left) is of little use. The patient should preferably collect sputum on rising in the morning in order to sample overnight secretions from the lungs (right). Specimens should be refrigerated if there is any delay in transport to the laboratory to minimize the overgrowth of oropharyngeal flora.

Other tests

Serology and PCR tests are available (**135**). These include the urine antigen for pneumococcus and *Legionella pneumophila* serogroup 1. PCR for viruses such as influenza A and B, parainfluenza, rhinovirus, metapneumovirus, and RSV are also available. Usually a throat swab preferably cut into viral transport medium (VTM) can be used as the sample (see Chapter 9, **149–153**). The availability and funding for these tests in primary care must be determined in conjunction with the local laboratory.

While the complement fixation test (CFT), a method of measuring antibodies to a particular organism, is being replaced by PCR, it may still be used for the diagnosis of a number of agents that cause 'atypical pneumonia' such as *Mycoplasma pneumoniae*, Q-fever, and psittacosis. A fourfold rise in antibody titre between paired acute and convalescent sera, taken 14 days apart is diagnostic. There are also specific IgM tests available for certain organisms such as mycoplasma.

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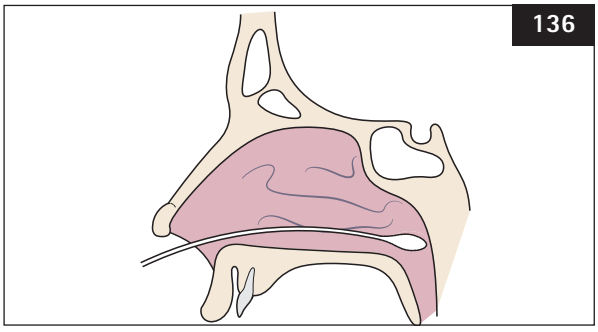
Staphylococcus aureus (MSSA)	Culture
Staphylococcus aureus (MRSA)	Culture
Streptococcus pneumoniae	Culture and urine antigen test
Haemophilus influenzae	Culture
Moraxella catarrhalis	Culture
Klebsiella pneumoniae	Culture
Mycobacterium tuberculosis	Microscopy for AAFB* and culture
Pseudomonas aeruginosa	Culture
Bordetella pertussis	Culture** or serology (single serum sample when cough is >3 weeks' duration***)
Chlamydophila pneumoniae	Serology, PCR
Legionella pneumophila	Urine antigen test (serogroup 1), and culture.
Mycoplasma pneumoniae	Serology for IgM antibodies, PCR
Coronavirus	PCR
Influenza virus A and B	PCR, immunofluorescence
Parainfluenza viruses	PCR, immunofluorescence
Metapneumovirus	PCR
Rhinovirus	PCR
RSV	PCR, immunofluorescence
Pneumocystis jirovecii	Microscopy of BAL**** (Sputum or EDTA blood for PCR)

*AAFB: alcohol acid fast bacilli; three 'early morning' sputum samples should be collected over several days for mycobacterial investigation.
In order to culture bordetella, specimen collection must be coordinated with the laboratory and paediatric department so that a pernasal swab can be 'plated out' immediately on agar selective for bordetella. The patient should be sent to the hospital to have the swab collected (see **136, 137).
***Serology for pertussis can be used, provided the last vaccination was at least 1 year ago. The test is useful for older children and adults with a chronic cough. Reports from the Respiratory and Systemic Infection Laboratory, HPA, Colindale state, as an example: '*Bordetella pertussis* anti-PT IgG: XXX IU/mL. In the absence of recent vaccination a titre of >70 IU/mL is consistent with recent infection.'
****Microscopy of sputum for pneumocystis has a low sensitivity; a bronchoalveolar lavage is done in the hospital setting. PCR can be done on sputum or EDTA blood. It would be appropriate to refer these patients to the infectious diseases physician.

135 Tests that can be used to diagnose respiratory tract infections; availability of PCR tests via local laboratories may vary.

136, 137 A pernasal swab mounted on a flexible wire for collection of organisms such as *Bordetella pertussis* from the nasopharynx should be inserted horizontally to clear the nasal turbinates, using the flexible wire swab. These specimens shoud be collected in the hospitals setting, so that the swab can be promptly inoculated onto the selective medium for growing pertussis.



Microbiological investigation of the patient with a chronic cough

In the individual with a chronic cough (over 3 weeks duration) as well as considering TB, a single blood sample may be sent for CFT but it must state on the request form the duration of the illness otherwise the sample will be treated as an 'acute sample', and stored while the 'convalescent' sample is awaited. Serology is useful when pertussis is considered. There has been raised awareness of adult pertussis in the setting of a chronic cough.[17] Serology can be used for diagnosis in older children and adults.[18] The test cannot be used if vaccination for pertussis has been given within the last year at least, as the antibody level within the year may represent the response to the vaccine.[18] This minimum period, and the 'cut-off' titre may differ between countries and advice through the local laboratory should be sought (see **135**). If a cough is less than 2 weeks duration, and pertussis is suspected, for example in a young child, a pernasal swab should be collected for culture. These patients should be referred to the local hospital paediatric department, who in liaison with the laboratory, can ensure that the correct sample is collected, and then promptly 'plated out' in the laboratory on the selective medium used for isolating *Bordetella pertussis* (**136, 137**).

The request form

In addition to full clinical details, additional tests should be specified. Examination for TB is one example, as laboratories usually only process specimens for mycobacterial culture when this test is stated on the request form, e.g. 'Ziehl–Neelsen (ZN) for AFB and culture for mycobacteria'.

The laboratory report

On reviewing the result, it is important to consider the relevance of the organisms identified in relation to those listed in **133**.

Interpretation of the results

Description of the sputum specimen as purulent or mucopurulent by the laboratory is important. Specimens with a salivary appearance should not be routinely cultured as they are unlikely to be representative of organisms at the site of infection. A specific pathogen, such as pneumococcus, can confirm the diagnosis, and the susceptibility profile directs further management. The presence of pseudomonas or 'coliforms' usually represents pharyngeal colonization, unless the patient has a chronic lung condition, such as bronchiectasis, cystic fibrosis, or advanced COPD. In the nursing home setting where there may be more debilitated patients who have had numerous courses of antibiotics, such organisms may cause infection. Once patients develop pseudomonas infection it can be difficult or impossible to eradicate. Mucoid strains are often associated with chronic lung disease.

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Staphylococcus aureus (MSSA)	Flucloxacillin or erythromycin
Staphylococcus aureus (MRSA)	Doxycycline with fusidic acid* or rifampicin*
Streptococcus pneumoniae	Amoxicillin or erythromycin
Haemophilus influenzae	Amoxicillin or co-amoxiclav or doxycyline or trimethoprim or azithromycin*
Moraxella catarrhalis	Co-amoxiclav or doxycycline* or azithromycin*
Klebsiella pneumoniae	Usually requires hospital treatment
*Mycobacterium tuberculosis***	Isoniazid, rifampicin, pyrazinamide, ethambutol (first-line agents)
Pseudomonas aeruginosa	Ciprofloxacin (note risk of CDAD due to *Clostridium difficile*)
Bordetella pertussis	Erythromycin, clarithromycin or azithromycin
Chlamydophila pneumoniae	Erythromycin, other macrolide or doxycycline*
Legionella pneumophila	(Usually requires intravenous therapy in hospital)
Mycoplasma pneumoniae	Erythromycin, other macrolide or doxycycline*
Coronavirus	None available
Influenza virus A and B	Oseltamivir* or zanamivir*
Parainfluenza viruses	None available
RSV	None available
Pneumocystis jirovecii	(Requires intravenous co-trimoxazole in hospital)

*Usual adult doses are:		
	Azithromycin	500 mg q24h day 1, then 250 mg q24h days 2–5
	Doxycycline	200 mg q24h
	Fusidic acid	500 mg q8h
	Oseltamivir	75 mg q12h (for 5 days)
	Rifampicin	600 mg q12h
	Zanamivir	10 mg puff twice q12h (for 5 days)

**Treatment always supervised by a chest physician or infectious diseases physician. It is important for the primary care physician when seeing the patient, confirms that the patient is taking all the agents prescribed for treatment.

138 Examples of oral treatment options for specific respiratory pathogens. Local susceptibility profiles must be considered.

Treatment

A summary of the treatment options to consider is given in the antibiotic guidelines in Chapter 11. In addition, further information on the treatment of lower RTI is shown in **138**.

If there is no response to treatment of a CAP within 48 hours, a wider range of organisms or antibiotic resistance should be considered, and advice, including hospital referral sought from the specialist hospital team.

TUBERCULOSIS

TB is a major issue. Pulmonary TB is relatively easily spread from the infected to uninfected individual(s), there are problems associated with its diagnosis and treatment, and the ever increasing threat of drug resistance underlines the importance of considering this infection in the individual with the chronic cough. This includes school children, those who may seem to be 'low risk' (**126**), and also health-care workers (HCW). Incidents occur in hospitals where it is only after weeks with the condition that the HCW with a chronic cough is considered to have pulmonary TB, which is confirmed with profuse AFB seen in sputum smears. Such an individual may have visited the primary care physician on several occasions, and TB was not considered. The 'look back' exercise that has to be conducted in the hospital where the HCW works is extremely time-consuming for the infection control team, and it is frustrating when one considers if the condition had been recognized sooner, this would have reduced the potential spread to many patients and other HCWs.

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Organism	Diseases usually associated with
Tuberculous – these are a public health risk	
Mycobacterium tuberculosis	Tuberculosis (pulmonary, miliary, etc.)
Mycobacterium bovis	Bovine pulmonary tuberculosis
Non-tuberculous – are not a public health risk	**All these organisms are ubiquitous in the environment**
Mycobacterium avium/intracellulare	Pulmonary disease in patients with pre-existing lung disaease (COPD, bronchiectasis), plus disseminated disease in HIV patients; AIDS-defining illness.
Mycobacterium chelonae	Can cause disease in the lung, skin, soft tissue, or bone in individuals who are immunocompromised or following trauma. A 'rapid grower'.
Mycobacterium kansasii	Chronic pulmonary lung disease simulating tuberculosis, can be disseminated in HIV patients. There is no person-to-person spread.
Mycobacterium malmoense	Pulmonary disease of patients with pre-existing lung disease.
Mycobacterium marinum	Skin and joint infections from salt or fresh water, especially of the hands in those who keep tropical fish. Considered to be more common in life guards as well. Can disseminate to other joints in the immunosuppressed individuals.

139 Mycobacteria are broadly grouped into the tuberculous and nontuberculous. Some features of important organisms are outlined.

The main learning points here are:

- To consider TB in any patient with an ongoing cough, particularly that of more than 3 weeks' duration. While the patient may have risk factors, such as ethnic origin, living in an area of high incidence, HIV disease, or alcoholism, there are patients with no clear and identifiable risk. The chronic cough may be the only clue.
- For microbiological investigation, three early-morning sputum samples must be submitted. Investigation for TB must be recorded on the request form.
- A positive smear of sputum (AFB seen) must prompt an immediate referral to the respiratory or infectious diseases physician who routinely manages TB.
- Negative smears do not exclude pulmonary TB, as microscopy is not as sensitive as culture. Note that specimens are cultured in liquid culture systems for 5–6 weeks.
- Patients with negative smears or who cannot produce sputum, and where TB is still strongly suspected, should be referred to the appropriate TB specialist.
- Patients diagnosed with TB should have an HIV test.
- Investigation of contacts is undertaken by public health. Notification of cases based on clinical diagnosis is the responsibility of the physician directly attending the patient.

Epidemiology

While there has been an increase in the incidence of TB in a number of countries, the distribution of cases can be highly variable. For example, within a reasonably large area of the UK, the number of cases is above the national average. However, if one examines the incidence across districts within this region, there are very few cases in certain areas, whereas the incidence in other areas is two to three times the national average. HIV disease has a significant influence, as the two infections often occur together. It is for this reason that patients with TB should have an HIV test.

Multidrug-resistant *Mycobacterium tuberculosis* (MDR-TB) is defined as an isolate that is resistant to at least isoniazid and rifampicin. Without these two drugs treatment is more difficult and less effective. A classification of important mycobacteria is shown in **139**.

Public health

It is the responsibility of the attending physician to refer the patient with a clinical diagnosis of TB to the respiratory/infectious diseases physician, and to notify cases diagnosed clinically to public health, who will then initiate contact tracing in the home, place of work, or recreational area such as a pub. Notification of the clinical diagnosis is important, while laboratory confirmation is awaited. Sputum specimens can be microscopy negative, and culture can take several weeks before a culture result is obtained. In the case of miliary tuberculosis, the patient will frequently not produce sputum. On occasion, a case is notified to public health, and subsequent culture identifies an environmental 'atypical' organism. The patient has to be 'denotified' at this stage. The inconvenience of doing this is far outweighed by the advantage of identifying the individual with open pulmonary TB at the earliest opportunity. It is good practice for the local laboratory to inform the attending physician, public health, and local TB team by some form of cascade of all new positive microscopy and culture results. An example of a 'TB cascade form' is shown in **140**. In addition to acting as an initial backup to ensure all relevant health-care professionals (HCP) are informed of a new case of tuberculosis, the form can be 'recascaded' from the laboratory when the antimicrobial susceptibility results show the organism is resistant to one or more of the agents being used in treatment. This is also a useful way of informing all concerned that an isolate that was suspected to be *Mycobacterium tuberculosis* is in fact an 'atypical' mycobacterium and the patient can then be 'denotified' for public health purposes.

Microbiology

Mycobacteria can be classified into two groups (see **139**):

- *Mycobacterium tuberculosis* complex, which includes *Mycobacterium tuberculosis* and *Mycobacterium bovis*.
- Atypical mycobacteria (also known as MOTT-mycobacteria other than tuberculosis). These organisms are found in the environment and are not communicable between individuals. They are of a lower pathogenicity and usually occur in patients with an underlying predisposition such as chronic lung damage. As these are environmental organisms, they should be cultured from sputum on at least two separate occasions to exclude *Mycobacterium tuberculosis*.

Mycobacteria have different staining characteristics from other bacteria due to the structural features of their cell wall, which are exploited by the ZN stain, with mycobacteria appearing as magenta-coloured bacilli. Other bacteria cannot resist decolourization by acid and alcohol and are therefore ZN negative. It is rarely possible to differentiate *Mycobacterium tuberculosis* from atypical mycobacteria by the ZN stain of a sputum.

Mycobacterium tuberculosis is slow growing, dividing every 18 hours or so, compared to a 'coliform' which divides about every 20 minutes. Most mycobacteria do not grow on routine laboratory media. In the past, culture was primarily performed on solid media, but is now done in liquid media. Other bacteria such as 'coliforms' can also grow, and if there are sufficient numbers of these contaminants, they will outgrow and overwhelm any mycobacteria present. For this reason, sputum specimens are treated with sodium hydroxide, which kills the contaminants, but the relatively more hardy mycobacteria survive. After neutralization of the alkali, the mycobacterial medium is inoculated. It is important that specimen of freshly collected sputum is sent to the laboratory promptly, but if there is any delay it is placed in the designated refrigerator. This will minimize the growth of contaminants, which can on occasion survive the decontamination process if they are present in large numbers, thus destroying a valuable specimen.

140

Department of Medical Microbiology, General Hospital.

CASCADE OF INFORMATION FOR A CASE OF PRESUMPTIVE TUBERCULOSIS:

This document cascades information about a new case of presumptive tuberculosis. **This is the first positive result on the patient from the laboratory (microscopy, culture or histopathology), and relevant information has already been communicated to the immediate clinical team or the primary care physician.**

Surname:	**First name:**
Hospital number:	**Date of birth:**
Address:	
Primary care physician/Practice:	
Request number(s): **Specimen type: Sputum, BAL, lymph node, urine, CSF, other [ ]**	
Date of collection:	**Date of receipt:**

MICROBIOLOGY

MICROSCOPY

☐ **NEGATIVE** ☐ **POSITIVE** **Date positive:……..……..**

RELATIVE NUMBERS OF AFB SEEN:

☐ **SCANTY** ☐ **MODERATE** ☐ **PROFUSE**

CULTURE

CULTURE POSITIVE ☐ **Date positive:……..……..**

CORDED: ☐ **YES** ☐ **NO**

(Note: If not corded this can represent a nontuberculosis mycobacterium)

HISTOPATHOLOGY REPORT

Reporting histopathologist: …….. **Date: ……..**

COPIES SENT TO:

Physician in charge:		**Primary care physician:**	
☐ **Lead TB physician** ☐ **ID physician**	**Hospital infection control team** ☐	**Public health dept.** ☐	**Community TB team** ☐

Reported by:	**Phone number:**	**Date:**

Update Comments (date added ……..):

140 A cascade form that can be used by the local laboratory to communicate information to all HCW involved in managing a patient with TB. In addition to acting as an initial backup to ensure all relevant HCW are informed of a new case, the form can be 'recascaded' from the laboratory when the antimicrobial susceptibility results show the organism is resistant to one or more of the agents being used in treatment. This is also a useful way of informing all concerned that an isolate that was suspected to be *Mycobacterium tuberculosis* is in fact an 'atypical' mycobacterium, and the patient can then be 'denotified' for public health purposes. (When mycobacteria grow in liquid culture, and ZN staining shows 'corded' clumps of organisms, this gives a reasonably good indication that the organism is likely to be identified as *Mycobacterium tuberculosis*.)

Specimen collection

Sputum

Release of mycobacteria from mucosal ulcers or loculated cavities in the lung is intermittent and irregular.[19] Therefore, the diagnosis of TB requires three (preferably early-morning) specimens to be collected on consecutive days, optimizing recovery of the organism (**141, 142**). A number of studies have demonstrated this. When only one specimen was submitted, about 60% of those that were culture positive were microscopy positive by the ZN stain, but when three specimens were examined this rose to 80%.[20] This is important to note, as a positive microscopy result is useful in the immediate management of the patient.

Specimens from other sites

TB can affect every organ system. From a practical perspective, most of the deep-seated infections are diagnosed in the hospital following, for example a tissue biopsy. On occasion, one early morning mid-stream urine (EMU) may be collected for the diagnosis of (renal) TB, or in the setting of miliary infection. Microscopy for AFB is not done on urine specimens, as resident nonpathogenic fast-growing mycobacteria such as *Mycobacterium smegmatis* can give a false-positive microscopy result.

Diagnosis of latent tuberculosis

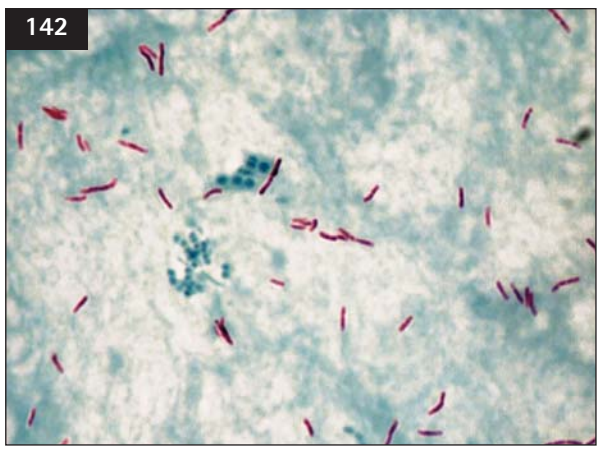
The diagnosis of latent TB in asymptomatic individuals has traditionally used the tuberculin skin test (TST), as either the Mantoux or Heaf tests. More recently, selective immunological (interferon gamma) tests (IGT) have been developed. These tests use antigens more specific for *Mycobacterium tuberculosis*, and are considered to remove false-positive results that may arise when using the TST. The result is better correlated with latent infection and dormant organisms, and there is little evidence of them being affected by prior bacillus Calmette–Guérin (BCG) vaccination.[21] There are various recommendations for the use of the TST and IGT tests which include initial testing with a TST, and then using the IGT test in those who are TST positive. These tests would be used by the local public health department in the screening of individuals who have been exposed to a case of open pulmonary TB.[21] Their use in primary care should be discussed with the local laboratory and the public health department.

Interpretation of results

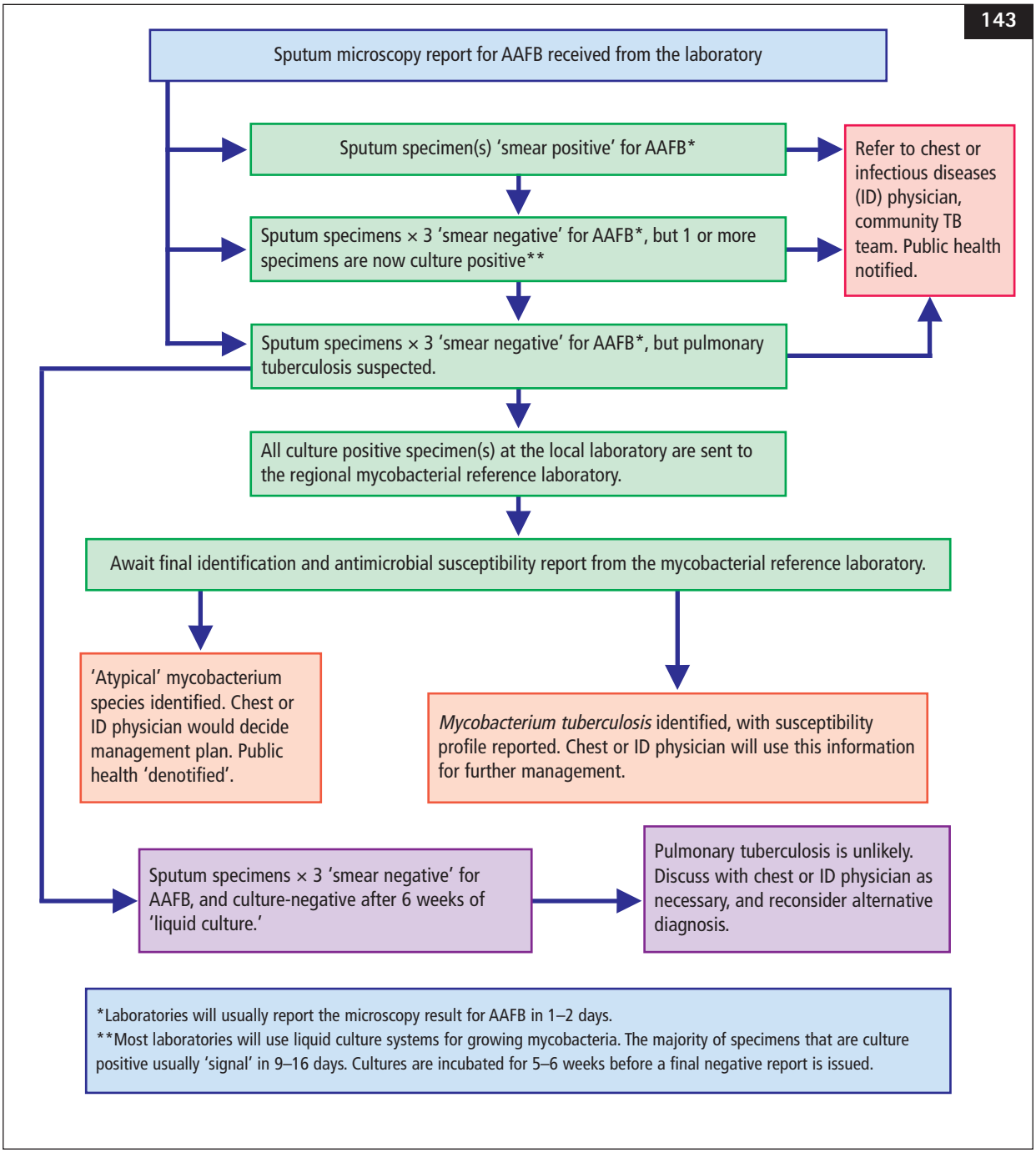
A flow diagram that summarizes the process from specimen collection to the final culture result is shown in **143**.

141

142



141, 142 (141) It is important that the patient with suspected pulmonary tuberculosis submits an early morning sputum specimen on 3 consecutive days in order to optimize a positive Ziehl–Neelsen microscopy result. (**142**) This sputum specimen shows a moderate number of magenta-stained mycobacteria in a sputum specimen of a patient with suspected pulmonary tuberculosis. This simple stain enables the correct care of the patient, as well as public health interventions, to be initiated promptly. Note the clumps of 'standard' bacteria that have only taken up the methylene blue counterstain. It is these oropharyngeal contaminants which may on occasion overwhelm the 'decontamination process' and overgrow the mycobacteria. This emphasizes the need for specimens to be refrigerated if they are not sent to the laboratory promptly.


143
Sputum microscopy report for AAFB received from the laboratory
Sputum specimen(s) 'smear positive' for AAFB*
Refer to chest or infectious diseases (ID) physician, community TB team. Public health notified.
Sputum specimens × 3 'smear negative' for AAFB*, but 1 or more specimens are now culture positive**
Sputum specimens × 3 'smear negative' for AAFB*, but pulmonary tuberculosis suspected.
All culture positive specimen(s) at the local laboratory are sent to the regional mycobacterial reference laboratory.
Await final identification and antimicrobial susceptibility report from the mycobacterial reference laboratory.
'Atypical' mycobacterium species identified. Chest or ID physician would decide management plan. Public health 'denotified'.
Mycobacterium tuberculosis identified, with susceptibility profile reported. Chest or ID physician will use this information for further management.
Sputum specimens × 3 'smear negative' for AAFB, and culture-negative after 6 weeks of 'liquid culture.'
Pulmonary tuberculosis is unlikely. Discuss with chest or ID physician as necessary, and reconsider alternative diagnosis.
*Laboratories will usually report the microscopy result for AAFB in 1–2 days.
**Most laboratories will use liquid culture systems for growing mycobacteria. The majority of specimens that are culture positive usually 'signal' in 9–16 days. Cultures are incubated for 5–6 weeks before a final negative report is issued.

143 An outline of the management process of the patient with suspected pulmonary TB after the patient has been asked to submit three early morning sputum specimens for microbiological examination to the local laboratory. The patient should have been given three sputum containers, plastic pouches for the containers, and three completed request forms marked 'TB microscopy and culture'. Clear instructions should be given to the patient about specimen collection, and the need to submit the specimen daily to the practice/clinic.

Treatment

Treatment of TB is the province of the respiratory or infectious diseases physician. Antituberculous drugs have to be administered for a prolonged period of months, and there can be toxicity. Interactions with other agents and antiviral regimes being used in HIV-infected individuals are a particular challenge, and it is for this reason that these patients will have ready access to the STI clinic as well. The primary care physician can be involved in managing other co-morbidities in the patient being treated for TB. At each visit, the physician should confirm compliance with the TB treatment, and be alerted by any signs of toxicity, such as in the liver. Noncompliance is an important reason for the emergence of drug resistance.

SUMMARY AND KEY POINTS

As raised in the Introduction, the microbiology laboratory may be considered to have a 'secondary' role in the management of day-to-day infections of the eye and respiratory tract. It is important that the primary care physician, in addition to contacting the relevant specialist team at the hospital, also contacts the medical microbiologist/infectious diseases physician when the patient's infection 'does not fit the norm'. TB and the unresolving pneumonia, the possibility of an underlying illness such as HIV, or risks associated with travel, occupation, pets, or recreation should prompt this dialogue. There can be a reliance of the primary care physician taking blood for serological investigation of an unresolving respiratory infection and requesting 'viral screen'. Such a request is unhelpful, and delays correct management of the patient.

Infection control in infections of the eye and respiratory tract is important. Adenovirus eye infections are highly contagious, and can be easily spread.[7] In addition to advising the patient on scrupulous hand washing, the attending HCW must also ensure that their hands are well washed, and all equipment used in examining the eye is either disposed or thoroughly decontaminated. Patients and young children in particular should be seen promptly, in order to minimize the chance of cross-infection in the waiting room.

In summary, the following points should be noted:

- The practice/clinic should establish guidelines for clinical and nursing staff to use so that there are set criteria, centred around the Quick Action Guides and the critical steps of **126**, and the management process for suspected pulmonary tuberculosis (**143**).
- These guidelines should be used regularly as a training tool on when and how to collect specimens in the various patient age groups, storage and transport of specimens, and how the laboratory report should be interpreted.
- When the patient with a CAP meets the criteria for admission to hospital, the first dose of the antibiotic should be given immediately. Even when it is considered that the patient can be treated at home, it is also reasonable to give the first dose of the antibiotic at the practice/clinic.

9

The Serology Specimen

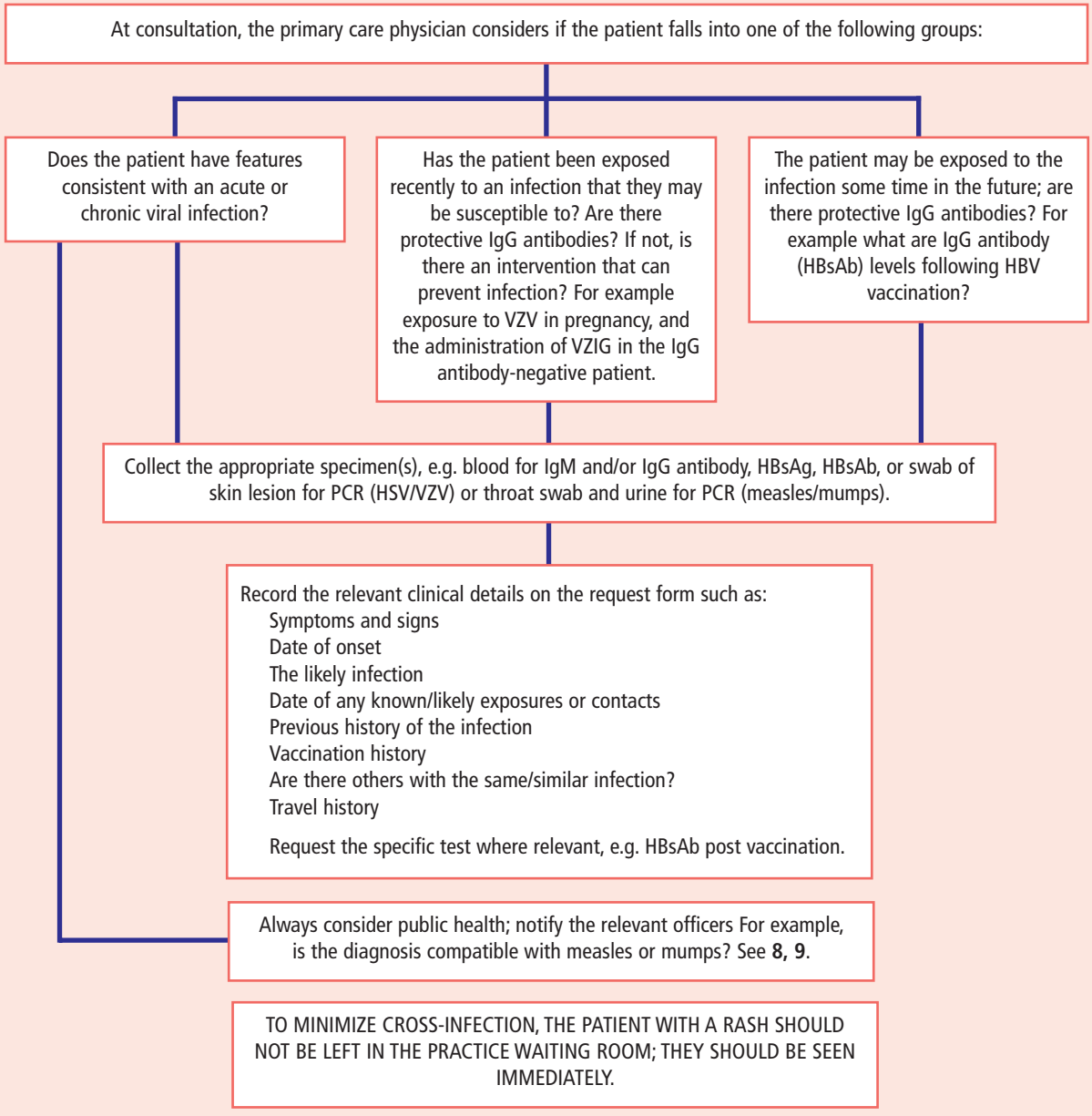
- Introduction
- How to get the most out of the laboratory
- Markers of infection
- Screening and determination of immune status
- Specimen collection
- Hepatitis viruses
- Management of sharps/slash injuries to members of the public
- Summary and key points

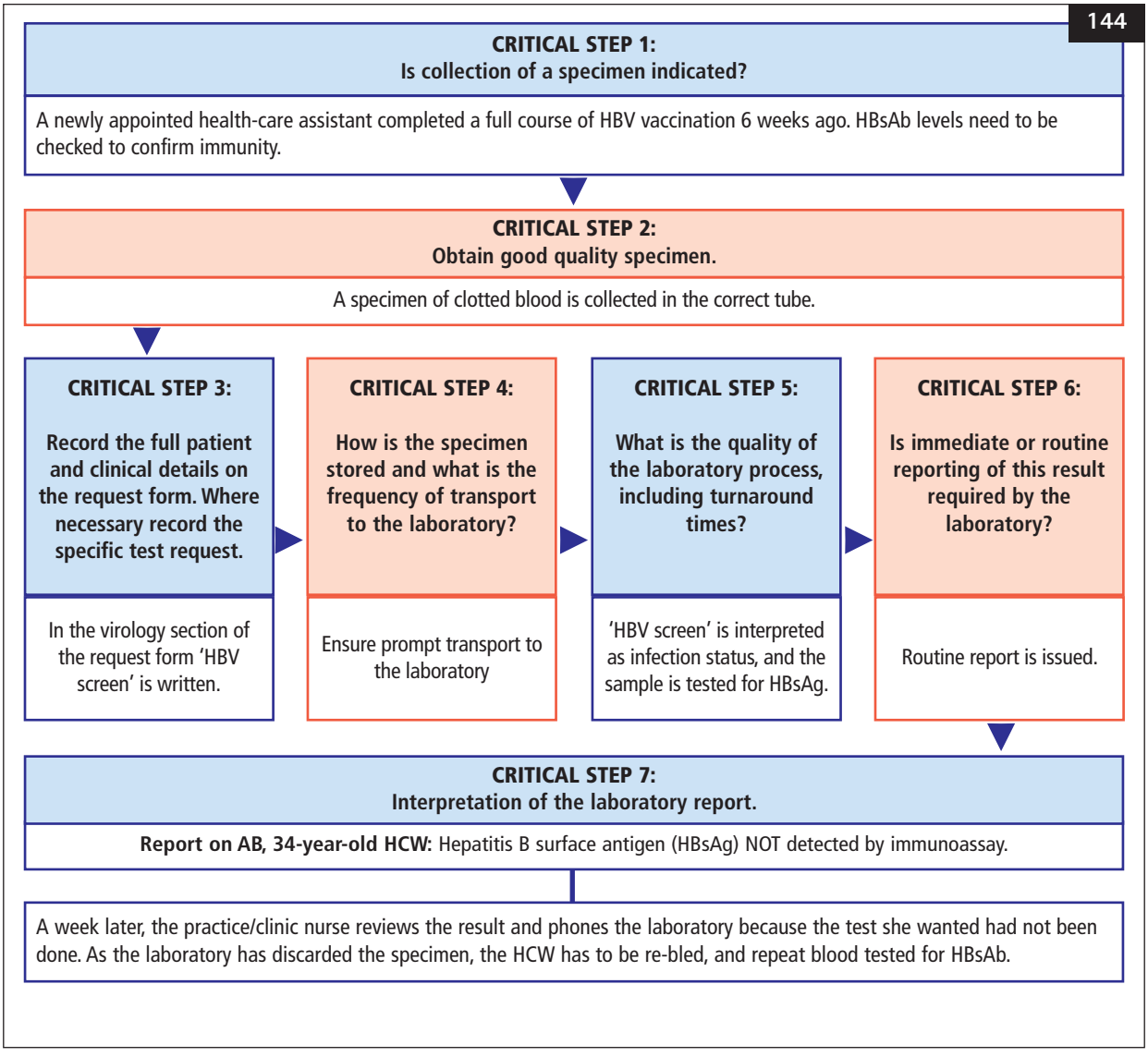
INTRODUCTION

The key to the serology specimen is providing clear and complete clinical details on the request form, in order to alert the laboratory as to the test(s) required on the specimen. A problem is shown in the scenario in **144**.

Quick Action Guide

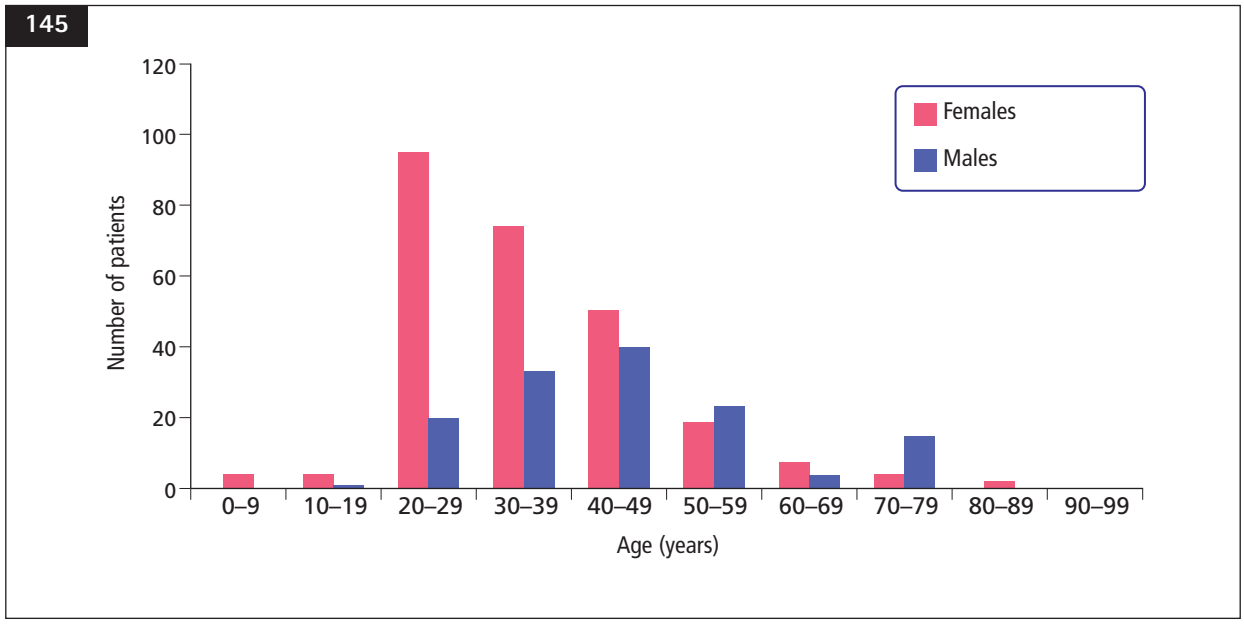
The serology specimen


At consultation, the primary care physician considers if the patient falls into one of the following groups:
Does the patient have features consistent with an acute or chronic viral infection?
Has the patient been exposed recently to an infection that they may be susceptible to? Are there protective IgG antibodies? If not, is there an intervention that can prevent infection? For example exposure to VZV in pregnancy, and the administration of VZIG in the IgG antibody-negative patient.
The patient may be exposed to the infection some time in the future; are there protective IgG antibodies? For example what are IgG antibody (HBsAb) levels following HBV vaccination?
Collect the appropriate specimen(s), e.g. blood for IgM and/or IgG antibody, HBsAg, HBsAb, or swab of skin lesion for PCR (HSV/VZV) or throat swab and urine for PCR (measles/mumps).
Record the relevant clinical details on the request form such as:
Symptoms and signs
Date of onset
The likely infection
Date of any known/likely exposures or contacts
Previous history of the infection
Vaccination history
Are there others with the same/similar infection?
Travel history
Request the specific test where relevant, e.g. HBsAb post vaccination.
Always consider public health; notify the relevant officers For example, is the diagnosis compatible with measles or mumps? See 8, 9.
TO MINIMIZE CROSS-INFECTION, THE PATIENT WITH A RASH SHOULD NOT BE LEFT IN THE PRACTICE WAITING ROOM; THEY SHOULD BE SEEN IMMEDIATELY.


144
CRITICAL STEP 1:
Is collection of a specimen indicated?
A newly appointed health-care assistant completed a full course of HBV vaccination 6 weeks ago. HBsAb levels need to be checked to confirm immunity.
CRITICAL STEP 2:
Obtain good quality specimen.
A specimen of clotted blood is collected in the correct tube.
CRITICAL STEP 3:
Record the full patient and clinical details on the request form. Where necessary record the specific test request.
In the virology section of the request form 'HBV screen' is written.
CRITICAL STEP 4:
How is the specimen stored and what is the frequency of transport to the laboratory?
Ensure prompt transport to the laboratory
CRITICAL STEP 5:
What is the quality of the laboratory process, including turnaround times?
'HBV screen' is interpreted as infection status, and the sample is tested for HBsAg.
CRITICAL STEP 6:
Is immediate or routine reporting of this result required by the laboratory?
Routine report is issued.
CRITICAL STEP 7:
Interpretation of the laboratory report.
Report on AB, 34-year-old HCW: Hepatitis B surface antigen (HBsAg) NOT detected by immunoassay.
A week later, the practice/clinic nurse reviews the result and phones the laboratory because the test she wanted had not been done. As the laboratory has discarded the specimen, the HCW has to be re-bled, and repeat blood tested for HBsAb.

144 Requesting a serology test in primary care. The steps in the process can be divided into seven critical steps. (See Chapter 1, 1.)
In this scenario, critical step 3 is breached, with inadequate information being recorded on the request form. 'HBV screen' is interpreted in the laboratory as screening for infection, for which the marker is HBV surface antigen (HBsAg); critical step 5. When critical step 7 is reached, this identifies the problem, wasting time and resources in repeat testing.
As post-vaccination immunity was required, the request form should have stated 'HCW completed course of HBV vaccine 6 weeks ago; immune status required' or 'HBsAb levels post vaccination'. The laboratory would do HBV surface antibody levels test based on this information.

Storing and transport of specimens for serology
Clotted blood should be collected in appropriate tubes. A full tube should be collected if possible, so that sufficient serum can be 'tapped off'. If there is a delay in transport, these specimens are refrigerated in the designated refrigerator.



145 The age and sex distribution of individuals having serological tests requested in primary care over a period of a week.

Examining the details of age and sex of patients recorded on several hundred consecutive serology request forms received from the community shows that the majority of tests are received from adult females between the ages of 20 and 39 (**145**). Patients may ask for their preconception immune status for rubella (and varicella zoster virus [VZV] occasionally), but the majority are for hepatitis B virus (HBV) immune status following vaccination (HBsAb), reflecting the fact that women in this age group dominate employment in the health-care services. Other tests include those for the diagnosis of acute infections of parvovirus B19, cytomegalovirus (CMV), Epstein–Barr virus (EBV), as well as acute and chronic hepatitis, and for human immunodeficiency virus (HIV). In addition to viruses, serological tests for infections caused by other organisms regularly requested include syphilis, leptospirosis, Lyme disease, and schistosomiasis. This chapter concentrates on antigen/antibody tests. However, it should be noted that serological tests such as the complement fixation test (CFT) for the agents that cause 'atypical' pneumonia are being replaced by more sensitive and practical polymerase chain reaction (PCR) tests that allow real-time diagnosis of an infection rather than the retrospective result provided by the 'paired specimens' that are used to obtain a meaningful CFT result.

HOW TO GET THE MOST OUT OF THE LABORATORY

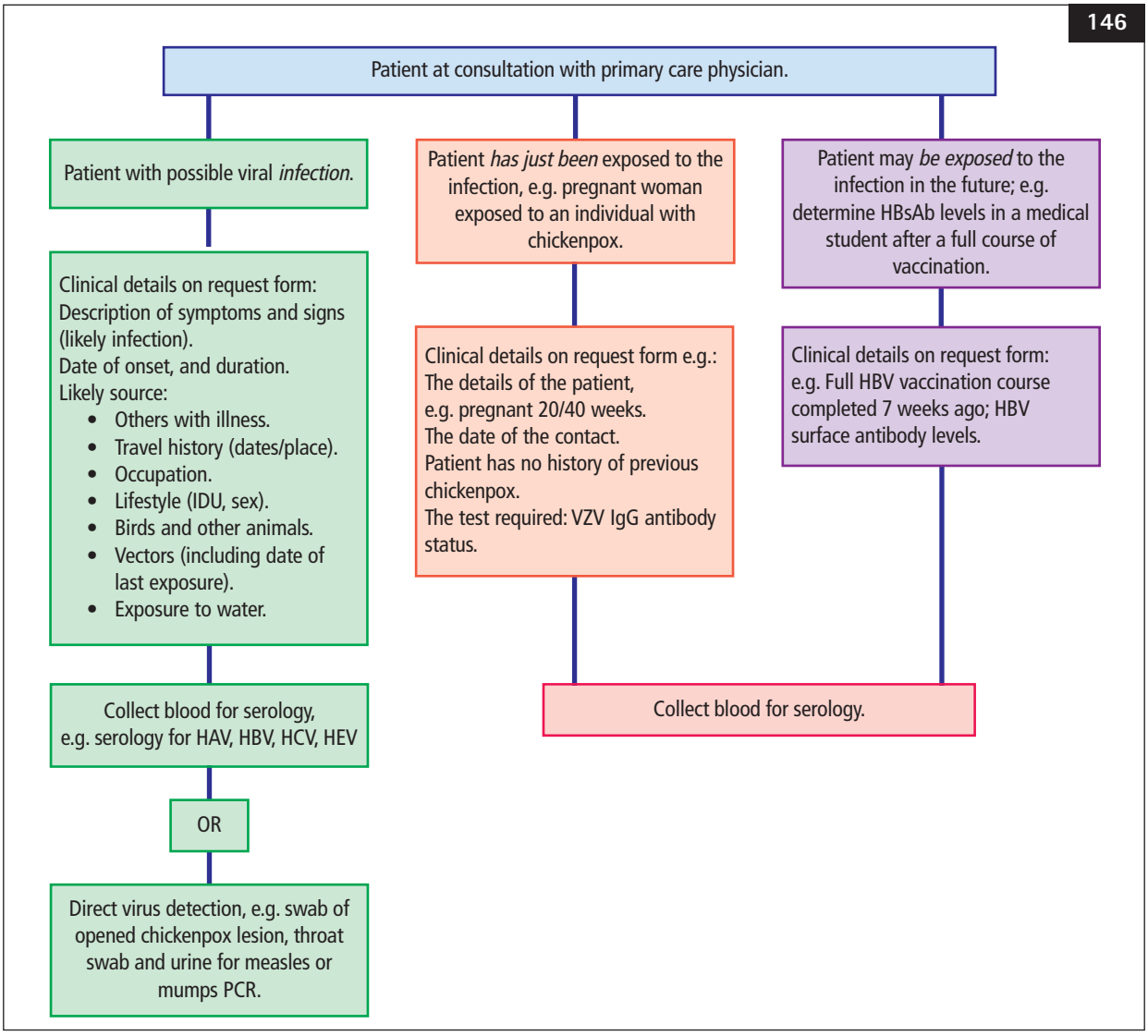
The routine request

The key to using the virology laboratory efficiently is to provide the full clinical details on the request form. It is unreasonable to expect the primary care physician to be familiar with the vast array of serological tests that are available, and to request the specific test(s) on all samples. Equally, the laboratory staff will not be able to decide which tests to do if the information is incomplete, or inadequate. For example, a common request is for a 'viral screen' with no other clinical details. This is not only unhelpful but it wastes a great deal of time as processing of the specimen can only occur when more clinical information is available. The term 'viral screen' by itself is meaningless as it provides no clue as to where to start with the large range of tests available. It is the responsibility of the requestor to provide the clinical information upon which the laboratory should perform the appropriate tests. The example given in **144**, where critical step 3 is breached, can occur fairly frequently, and wastes both time and resources. The request form box in the Quick Action Guide should be referred to.

Knowledge of the incubation period for an organism is sometimes necessary when requesting a serological test. The minimum incubation period for leptospirosis is 5 days, and IgM antibodies are

then detectable several days later. A request for the serological diagnosis of leptospirosis which states 'fell into canal 2 days ago' is not appropriate. The asymptomatic traveller exposed to water-borne shistosomiasis in sub-Saharan Africa should not be tested for antibodies to the parasite until 3 months after the last exposure, as the diagnostic test uses egg antigen, and it takes a minimum of 6 weeks before the female parasite initiates egg production. By giving the relevant dates of exposure, the laboratory can at least inform the requestor if the sample was taken too early. If no dates were given, the sample might be processed leading to a potentially false-negative result.

A summary of the process of test selection and the details to put on the request form is shown in **146**. Hepatitis A, B, C, and E (HAV, HBV, HCV, HEV) are discussed further in the chapter for the reader who is interested in the details of the markers of infection of these viruses. The blood-borne viruses (BBVs) HBV, HCV, and HIV are important examples where serology is key to identifying 'silent', chronic infection. This is highlighted in Chapter 10, **170, 171**, where identification of HIV in pregnancy and the use of antiviral therapy have such a dramatic effect in reducing transmission to the child.


146
Patient at consultation with primary care physician.
Patient with possible viral *infection*.
Patient *has just been* exposed to the infection, e.g. pregnant woman exposed to an individual with chickenpox.
Patient may *be exposed* to the infection in the future; e.g. determine HBsAb levels in a medical student after a full course of vaccination.
Clinical details on request form:
Description of symptoms and signs (likely infection).
Date of onset, and duration.
Likely source:
• Others with illness.
• Travel history (dates/place).
• Occupation.
• Lifestyle (IDU, sex).
• Birds and other animals.
• Vectors (including date of last exposure).
• Exposure to water.
Clinical details on request form e.g.:
The details of the patient, e.g. pregnant 20/40 weeks.
The date of the contact.
Patient has no history of previous chickenpox.
The test required: VZV IgG antibody status.
Clinical details on request form:
e.g. Full HBV vaccination course completed 7 weeks ago; HBV surface antibody levels.
Collect blood for serology, e.g. serology for HAV, HBV, HCV, HEV
OR
Direct virus detection, e.g. swab of opened chickenpox lesion, throat swab and urine for measles or mumps PCR.
Collect blood for serology.

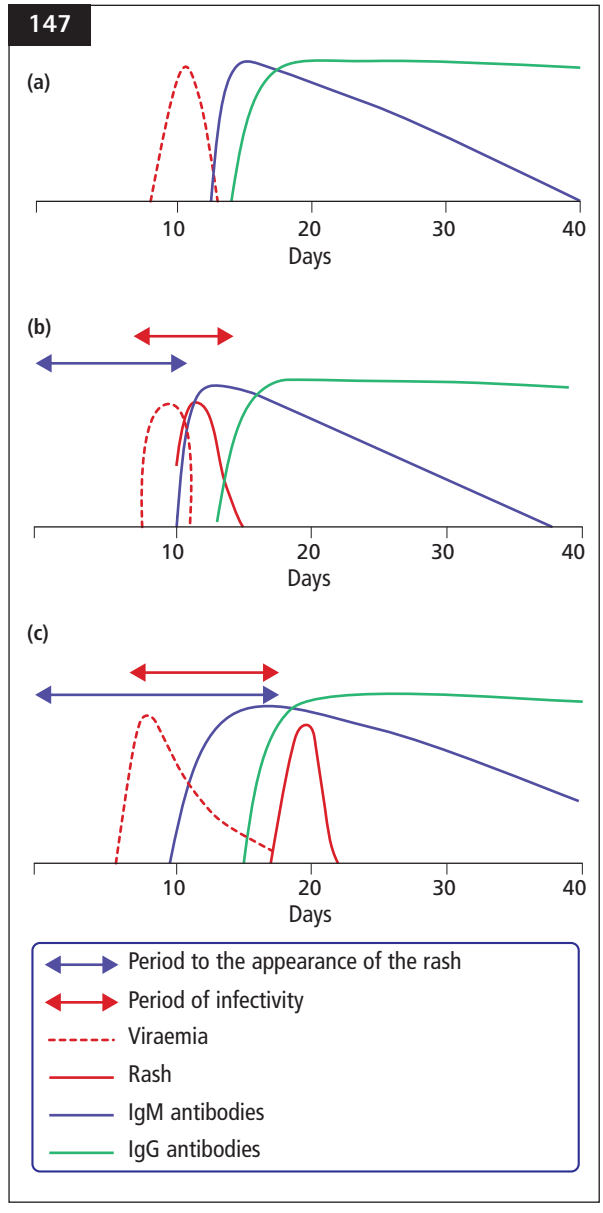
146 Following review of the patient, the necessary tests will be considered. It is important to give the full clinical details on the request form, so that the laboratory can select the correct test.

The urgent request

The primary care physician is responsible for recognizing urgent situations, and the need for a sample to be tested immediately in the laboratory, so that the result can be used to manage the patient. Exposure to VZV in pregnancy is an example, as varicella zoster immunoglobulin (VZIG) prophylaxis needs to be administered within 10 days of exposure in order to protect the mother and her fetus/newborn. Not infrequently the patient presents late in this 10-day window period, leaving little time for action. In these circumstances, the primary care physician must phone the medical microbiologist/virologist to alert them of the situation, so that the specimen can be submitted, tested, and if needed, VZIG administered, promptly. Chapter 10, **165**, should be referred to.

MARKERS OF INFECTION

The appearance of markers of a 'typical' virus infection is shown in **147**. There is an incubation period during which the virus is multiplying in a particular tissue, followed by a release of the virus into the bloodstream (viraemia), allowing the virus to reach the target organ, which in the case of VZV is the skin. IgM antibodies appear towards the end of the viraemia, followed by IgG antibodies (**147a**). With VZV, there is a minimum incubation period of about 10 days before appearance of the diagnostic rash (**147b**). Forty-eight hours before the rash appears, there is the (viraemic) prodromal period (fever and malaise), when virus is excreted via the lungs (**147b**). Virus excretion from the lungs occurs earlier than the skin rash because the virus can migrate much quicker through respiratory tissue as opposed to skin which is composed of multiple layers of cells. The individual is regarded as being infectious from the beginning of the prodromal period (48 hours before the rash appears) until the rash crusts. The diagnosis of chickenpox is usually made clinically. Where confirming the diagnosis is important or is uncertain, vesicle fluid should be sent for VZV PCR. The presence of VZV IgM antibodies can also be used to confirm acute infection but detection of virus is the preferred option. Unlike the situation with VZV, where the prodromal period runs into the appearance of the rash, with parvovirus B19 there is a biphasic process. The prodromal period, which is often asymptomatic, occurs 6–9 days after infection, and is followed some days later by the appearance of the rash (**147c**). The individual is considered to be infectious from the prodromal period to the appearance of the rash. Because of the gap between the often asymptomatic, viraemic stage, and the rash, IgM antibodies are present when the rash appears making detection of acute infection by parvovirus IgM a useful diagnostic tool. The specific features of VZV and parvovirus B19 infection



147 The time course of events of a virus infection presenting with a rash. (**a**) After an incubation period, there is a viraemia, when the individual would be considered infectious, followed by the appearance of IgM and IgG antibodies. Virus may be detected by the presence of live virus, a viral antigen, or the genome (DNA or RNA). (**b**) With VZV, the rash appears after an incubation period of 10–21 days; the infected individual has been infectious for 2 days before the rash appears (prodromal period). (**c**) With parvovirus B19, the rash appears after an incubation period of about 18 days; the individual is considered infectious from the beginning of viraemia to the appearance of the rash.

outlined in **147** are important in managing the nonimmune woman exposed during pregnancy (Chapter 10).

Other factors may need to be taken into account. With Lyme disease, prompt antibiotic prescription after a tick bite can diminish the antibody response. It should also be noted that with many viral infections, the acute infection is often subclinical, especially in children; HAV and HBV are examples of this.

Other markers of infection

Nonspecific markers of infection are used in the diagnosis of certain organisms. These include the Monospot Test, where heterophile antibodies that react with horse red blood cells is consistent with acute EBV infection, and the venereal disease research laboratory/rapid plasma reagin (VDRL/RPR) test in syphilis. VDRL antibodies react with cardiolipin, and can be present in primary, secondary, and reactivated infection, when there is active disease. Along with clinical symptoms and signs, the various serological markers are used to define the various stages of syphilis infection (Chapter 10, **173**, **174**).

Figure **148**, outlines the tests that can be used to identify acute and chronic infection, or determine the immune status of an individual. Note that there

148

	Infection			Immune status	Screen
	Acute	Chronic (latent/reactivated)			
Hepatitis A*	IgM			✔	✘
Hepatitis B*	cIgM	sAg/cIgG	(C)	✔ (HBsAb)	✔
Hepatitis C*	(RNA)*	RNA	(C)	✘	(✔)
Hepatitis E*	IgM			✘	✘
HIV	p24 Ag and Ab (RNA)		(A/C)	✘	✔
Mumps	IgM**			✔	✘
Measles	IgM**			✔	✘
Parvovirus B19	IgM			✔	✘
Rubella	IgM			✔	✔
VZV	IgM***	Herpes zoster***		✔	✘
EBV	Various	(R)****		✘	✘†
CMV	IgM	(R)****		✘	✘†
Leptospirosis	IgM			✘	✘
Lyme disease	IgM, (IgG)		(A/C)	✘	✘
Treponema	VDRL, Treponemal IgM	Treponemal Ab, TPPA	(A/C/L/R)	✘	✔
Helicobacter		Faecal antigen	(C)	✘	✘
Toxoplasmosis	IgM	IgM/IgG	(L/R)	✘	[✔]
Schistosomiasis		IgG††	(C)	✘	✘

Note that other tests can be used to diagnoses acute infection, e.g. PCR on throat swab or urine for measles or mumps.

*For the relevant markers, see **155–164**;

**PCR can be done using a throat and/or urine to diagnose acute infection;

***If the clinical diagnosis in not clear, PCR of vesicle fluid is the 'gold standard';

****Reactivated disease is an important consideration in immunocompromised patients;

†Screening for past infection is done in for certain patient groups, for example donors and recipients before renal transplantation;

††Examination of urine and stool for ova is also done (see Appendix).

✔Test done as considered necessary/appropriate.

✘Test not done as usually not appropriate.

(✔) Screening for HCV would be done in high-risk groups, such as a community health service for IDU.

[✔] In certain countries, screening for toxoplasmosis is done.

Infection: A: acute; C: chronic; L: latent; R: reactivation. (See Appendix for further information on each organism.)

148 A list of organisms for which serological tests can be used to determine if the patient has an acute, or chronic infection, their immune status based on the presence or absence of protective IgG antibodies, or for screening patients in certain groups (for example, antenatal screening for HIV, HBV, rubella, and syphilis, and HCW for measles mumps, rubella, and VZV immunity). See Appendix, Chapter 9 for more detailed information.

is some overlap in the use of the terms 'immune status' and 'screen' as used here. (The organisms listed in **148** are discussed in more detail in the Appendix to this chapter).

SCREENING AND DETERMINATION OF IMMUNE STATUS

Screening

This term is used for individuals in a particular risk group who may either be susceptible to a particular infection, or they are 'silent' chronic carriers. The most pertinent example is routine screening done at the first antenatal visit for HIV, HBV, rubella, and syphilis. These results are used, as appropriate, to manage the mother during her pregnancy, and protect the fetus and newborn from congenital or perinatal infection.

The request form should state the specific circumstances for screening. With the pregnant woman presenting at her first antenatal visit, the clinical details should be, for example, 'Pregnant, 13/40 weeks, antenatal booking blood for HBV, HIV, rubella, and syphilis status'. Appropriate advice and consent would be given before the specimen is collected. When the results of these tests are available, they should be recorded clearly in the patient's notes. It is also worthwhile to ask the patient at the first visit if she has had chickenpox in the past. A record of definite previous infection should be recorded, and if exposure to chickenpox occurs in the pregnancy, reassurance only is required. If there is no history, then information should be given about seeking medical advice as soon as practicable after exposure.

The status of pregnant woman at antenatal screening can be:

- Immune, where protective IgG antibodies are DETECTED (or reported as POSITIVE); this applies to rubella.
- Susceptible, where protective IgG antibodies are NOT DETECTED (or reported as NEGATIVE), this applies to rubella. The woman is susceptible, and should be given rubella vaccine after the baby is born.
- Not infected (NEGATIVE/NOT DETECTED); the absence of HIV antigen/antibody, the absence of HBV surface antigen (HBsAg), and the absence of treponemal antibodies shows no serological evidence of infection at that point in time.
- Infected (POSITIVE/DETECTED); the presence of HIV antigen/antibody, the presence of HBsAg, or the presence of treponemal antibodies shows serological evidence of infection at that point in time, and thus the potential for congenital or perinatal transmission.

It is very important to collect a second blood from the pregnant patient to confirm the result of a positive HBV, HIV, or syphilis test. Errors do occur on occasion at specimen collection, labelling the request form, or in the laboratory. The consequences of an error not being identified, as a result of a second specimen not being submitted, could clearly be devastating for another individual as well.

Determination of immune status

This term is used to determine whether or not the individual has protective IgG antibodies to a particular agent. This information can be used:

- To determine if the individual just exposed to an infection is susceptible. This is determined by testing to see whether or not they have protective IgG antibodies. It is essential that these situations are managed promptly within the incubation period of the virus, in order that any effective interventions can be instituted. The request form must state the specific circumstances of the exposure.

  Consider the following example:

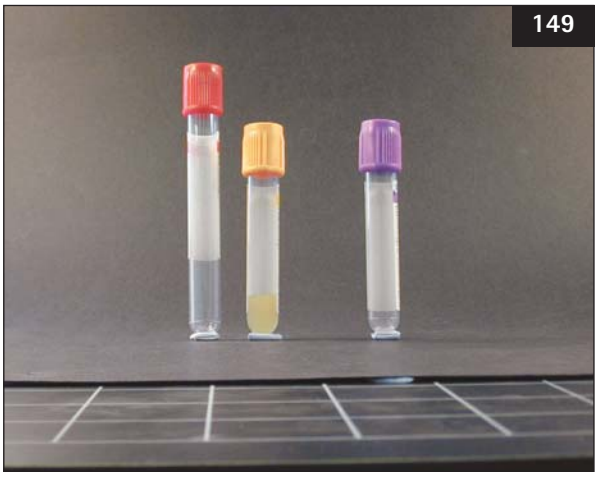
> Teacher, pregnant 16/40 weeks, in contact with a child in class who developed chickenpox 7 days ago. No history of chickenpox in the past. VZV immune status required.

Taking into account the prodromal period of 2 days, during which the child would have been infectious, it is now 9 days since the first exposure. As VZIG needs to be given within 10 days of exposure, there is now a sense of urgency for all concerned, centring on the test being done to determine her immune status.

- To determine whether or not the individual who may be at risk in the future has protective IgG antibodies or not. The request form should state the specific circumstances, for example 'New practice/clinic nurse, completed HBV vaccine course 6 weeks ago'. The laboratory will know to test for HBsAb.

SPECIMEN COLLECTION

Primary care staff should liaise with the local laboratory regarding the tubes to use for serology or PCR tests on blood. When swabs are taken from skin lesions for herpes simplex virus (HSV) and VZV PCR, or from the throat for respiratory virus PCR, they should be cut into a sterile container, preferably containing viral transport medium (VTM). However, as the logistics of having an 'in date' stock of VTM in the practice/clinic means that laboratories will usually accept a dry swab alone (**149–153**). However, one should check with the



149–153 (149) An example of the tubes used for serology/virology tests. For viral PCR tests, EDTA tubes should usually be used. **(150)** Swabs are used for collecting a specimen for PCR, such as a suspected herpes lesion. A sterile standard container with VTM should preferably be available. **(151)** After collection the swab is cut into the container. **(152)** If VTM is not available, cut the dry swab into the container. (A supply of sterile scissors should be available to use, so that there is no chance of contaminating the scissors when cutting the swab, after for example taking a throat swab). **(153)** A sample of 5–10 mL of urine can be collected for PCR, e.g. measles and mumps, along with a throat swab.

local laboratory as to how they want to receive specimens. After taking a throat swab, it is prudent to use sterilized scissors to cut the shaft of the swab, or, as a very minimum, ensure that they are cleaned well afterwards with an alcohol wipe. PCR tests are very sensitive, and any cross-contamination may occur when collecting specimens from different patients, producing a false-positive result. Urine (5–10 mL) for PCR should be collected into a sterile white-topped container (see Chapter 3, **47–52** for urine collection methods). The availability of tests, such as PCR for measles and mumps, should be confirmed with the local laboratory. These tests are very useful for infections that are usually uncommon, and the physician is not familiar with the clinical presentation of the illness.

HEPATITIS VIRUSES

Tests for HAV, HBV, and HCV should be done for all cases of hepatitis; in addition CMV and EBV should be considered in the adolescent or young adult when the above tests are negative. HEV is usually thought to be acquired following travel to endemic parts of the world such as southeast Asia, the Indian subcontinent, or Africa. However, sporadic cases that are likely to have been acquired locally are reported, and testing for HEV should be considered when the other hepatitis viruses have been excluded. Important features of these viruses, and markers used in their diagnosis are given in **154** and **155**. Serology is used to identify acute infection (HAV, HBV, HEV), chronic infection (HBV), natural immunity (HAV, HBV), and vaccine-derived

154

Virus	Incubation period Usual (range)	Transmission	Acute	Chronic	Complications	Comments
HAV (SS-RNA)	45 (20–60 days)	F/O	Y	N	Acute liver failure (ALF)	Infection confers immunity
HBV (DS-DNA)	60–90 (45–180 days)	Blood-borne	Y	Y	ALF, cirrhosis, HCC	HBsAb confers immunity
HCV (SS-RNA)	60–90 (45–180 days)	Blood-borne	Y	Y	Cirrhosis and HCC	No natural immunity
HEV (SS-RNA)	45 (20–60 days)	F/O	Y	N	ALF	5 genotypes
CMV (DS-DNA)	Several weeks	Saliva/ respiratory	Y	Y	Acute and reactivated infection is important in pregnancy and the immunocompromised patient.	
EBV (DS-DNA)	Several weeks	Saliva	Y	Y	(Reactivated infection is important in the immunocompromised).	

F/O: faecal–oral route of transmission.
SS: single-stranded; DS: double-stranded.
ALF: acute liver failure.
HCC: hepatocellular carcinoma.

154 The viruses associated with acute and chronic hepatitis, and important features of each virus.

immunity (HAV, HBV). With HCV, antibody tests are of no use on their own. All patients who have been infected will have antibodies. However, as some individuals clear the virus a second test for the presence or absence of viral ribonucleic acid (RNA), determined by reverse transcriptase PCR (RT-PCR), must be done. Patients who are antibody positive but in whom virus cannot be detected by PCR require no further treatment as they have eradicated the virus. Figure **156**, page 162, shows key structural features of HAV, HBV, HCV, and HEV. Note that all cases of viral hepatitis, acute or chronic are notifiable to public health.

HAV

HAV is a single-stranded RNA picornavirus, and is transmitted mainly from person to person via the faecal–oral route.[1] Although there are a number of genotypes, there appears to be only one serotype of the virus.[2] Travel to underdeveloped parts of the world carries a risk. Transmission is possible by contaminated water or food, including fresh fruit and vegetables and undercooked molluscs (these are filter feeders and if in the vicinity of sewage outlets will concentrate the virus). Outbreaks occur in other groups and include men who have sex with men (MSM).[3] Unusual outbreaks have occurred in intravenous drug use (IDU), with drug packages being couriered rectally to avoid detection.

155

Virus	Acute	Past infection	Natural immunity	Chronic infection
HAV	HAV IgM (IgG) (**157**)	HAV IgG (**157**)	HAV IgG (**157**)	Not known
HBV	HBcIgM (**159**)	HBcIgG (**160**)	HBsAb (**160**)	HBsAg+, HBeAg+ (High risk)* (**160, 161**) HBsAg+, HBeAb+ (Low risk)* (**160, 161**)
HCV	HCV RNA** (**163**)	HCV antibody (**163**)	Not conferred by infection There are 6 genotpes	HCV RNA detected
HEV	HEV IgM (IgG) (**164**)	HEV IgG (**164**)	There are 5 genotypes	Not known (?)
CMV	CMV IgM Atypical lymphocytes	CMV IgG	N/A	(Relevant in the immunosuppressed)
EBV	Monospot positive Atypical lymphocytes	EBV IgG to NA (EBNA) (NA: nuclear antigen)	N/A	(Relevant in the immunosuppressed)

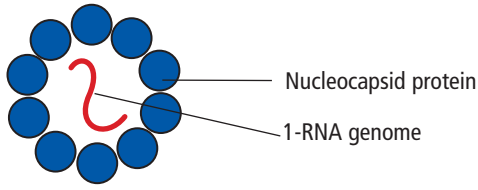
*Patients with chronic infections should be managed by the hepatologist. Patients who are HBsAg positive, but who are negative for both HBeAg and HBeAb should be considered as 'high-risk' until their viral DNA status has been determined.

**HCV RNA: note that acute HCV disease is not often recognized, as acute infection is usually asymptomatic.

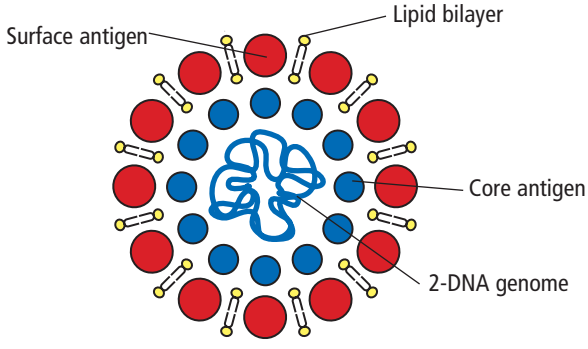
155 The serological and nucleic acid markers used in the diagnosis of viral hepatitis. Numbers refer to relevant Figure (**157, 159–164**).

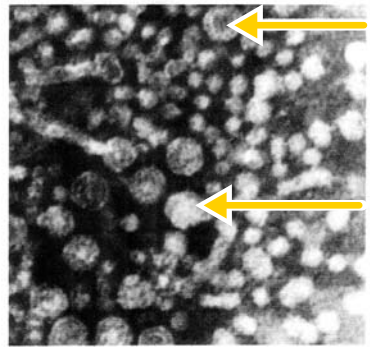
156

(a)

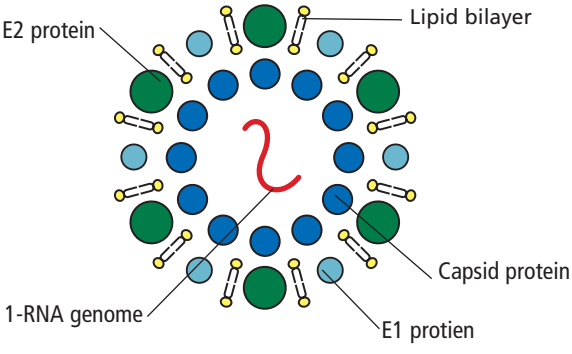

Nucleocapsid protein
1-RNA genome

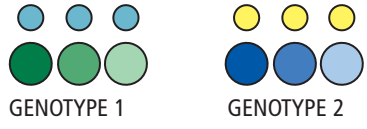
(b)


Surface antigen
Lipid bilayer
Core antigen
2-DNA genome

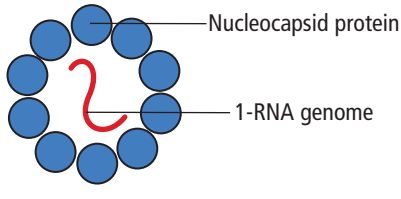


(c)


E2 protein
Lipid bilayer
Capsid protein
1-RNA genome
E1 protien

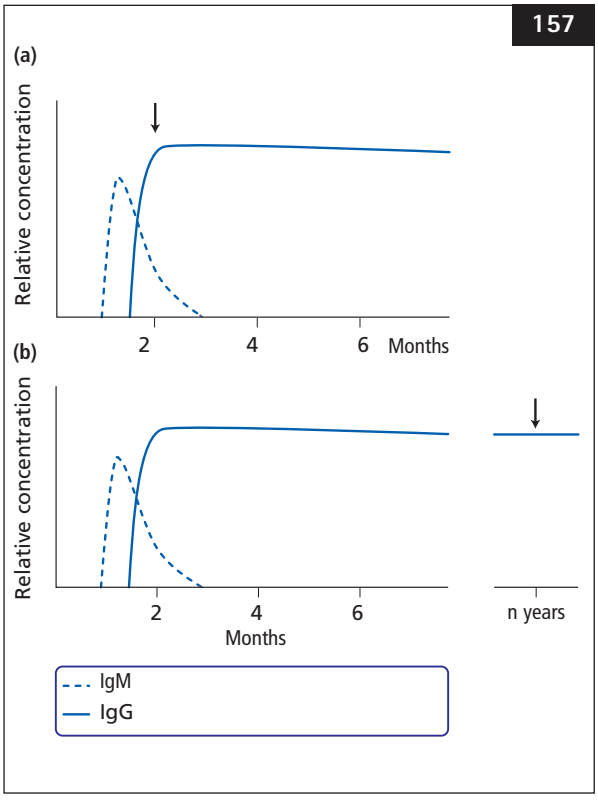

GENOTYPE 1
GENOTYPE 2

(d)


Nucleocapsid protein
1-RNA genome

The habit of licking the tin-foil wrapping of a consignment previously concealed in the rectum of a courier who has acute HAV has transmitted the virus! One outbreak was tracked back to an individual who was employed to pick fruit at harvest time. Pickers are paid by the weight of fruit picked. The individual in this instance urinated on the fruit to increase the weight of the fruit and thus his financial remuneration. Unfortunately for the people who ate the fruit he was incubating hepatitis A. This is an unusual example, but shows that in the viraemic patient virus also enters the renal tract, which would not be the usual route of transmission, and that infections can be transmitted from person to person in every conceivable way!

Most infections are asymptomatic, especially in children.[4] The incubation period is about 45 days (range 20–60), followed by the acute infection which is diagnosed serologically by the detection of HAV IgM antibodies; these may be present for 6–10 weeks after the acute infection. Individuals are infectious 2 weeks before symptoms and signs appear, but then rapidly become noninfectious. IgG antibodies appear, and give natural immunity for life. IgG antibodies produced by vaccination also give protection for life (**157**).



157 The appearance of HAV IgM and IgG antibodies. **(a)** Patient with acute hepatitis. HAV IgM antibodies detected, evidence of acute infection. IgG antibodies can also be detected at this time. **(b)** Patient requests to have their immunity to HAV determined for travel reasons. IgG antibodies are detected showing natural or vaccine-induced immunity.

156 **(a)** HAV has a single serotype. IgG antibodies that are produced to the capsid proteins following infection, or immunization, provide long-lasting immunity. **(b)** The electron micrograph shows a purified preparation of HBV obtained from an infected patient. (adapted from website of PHIL, CDC, Atlanta, with permission). An intact (lower arrow) and damaged virus particle (upper arrow) are seen; in the latter, the two protein shells made up of HBsAg (outer) and HBcAg (inner) can be clearly seen. A vast excess of surface antigen is produced during virus replication, which aggregates into filaments and spheres. (See **159–161**). **(c)** HCV has a capsid surrounding the 1-RNA genome. There are two surface proteins E1 and E2. A region in the gene coding for E2 protein gives rise to an epitope to which potentially neutralizing antibodies are produced. However, this gene is hypervariable, and the antigenic epitope is continually changing, giving rise to a heterogenous antibody response that is unable to neutralize the virus. In addition, there are six genotypes and 22 subtypes which further increase the antigenic diversity. **(d)** HEV consists of a 1-RNA genome surrounded by the capsid protein. IgM antibodies to the capsid proteins are produced and are the marker of acute infection. IgG antibodies show past infection.

HBV

HBV is a member of the Hepadnaviridae, and has a double-stranded deoxyribonucleic acid (DNA) genome. Despite having a relatively small genome, HBV has a complex replication cycle which uses reverse transcription.[5] The virus is mainly blood-borne, but is also found in genital tract secretions. Other routes of transmission include perinatal infection, from an infected patient to a health-care worker (HCW) and *vice versa* as 'sharps injuries', IDU, and sexual intercourse.

Three proteins and the antibodies produced to them, are used as markers of infection. These are surface antigen (HBsAg), core antigen (HBcAg), and e antigen (HBeAg) (**156**). The HBsAg, embedded in a lipid bilayer, makes up the outer protein shell of the virus. When HBsAg is detected in the blood of an individual, that person is infectious, with active virus replication taking place in the liver. Therefore, the first test done for HBV infection is the HBsAg test; if this is negative, no further tests are done in most circumstances. The HBcAg makes up the inner protein shell of the virus; this protein is extremely immunogenic, and IgM antibodies are the marker of acute infection. HBcAb (IgG) antibodies are then produced, and although not protective, are life-long indicators that the individual has been infected with HBV at some time. HBeAg is a nonstructural protein produced during replication and is a 'crude' marker of the degree of virus replication in the liver. Individuals who are HBsAg and HBeAg positive are considered 'high risk', whereas those who are HBsAg positive and HBeAb positive are usually considered 'low risk'. The main markers used to determine the status of an individual are shown in **158**, and these should be referred to when considering **159–161**.

158

HBsAg*	HBsAb	Anti-HBc (Total core antibody)	HBcIgM	Comment	Figure
Negative	(Negative)**	(Negative)**	(Negative)**	No HBV infection	**159A**
POSITIVE	Negative	Negative	Negative	Very early acute infection	**159B**
POSITIVE/ Negative***	Negative	POSITIVE	POSITIVE	Acute infection	**159C**
Negative	Negative	POSITIVE	Negative	Window period	**160D**
Negative	POSITIVE	POSITIVE	Negative	Previous infection and immunity	**160E**
POSITIVE	Negative	POSITIVE	Negative	Chronic carriage	**160F** **161**
---------- (To be done	POSITIVE NEGATIVE****	---------- To be done	---------- ----------	Post vaccination Post vaccination****)	**162** G, G' **162** H

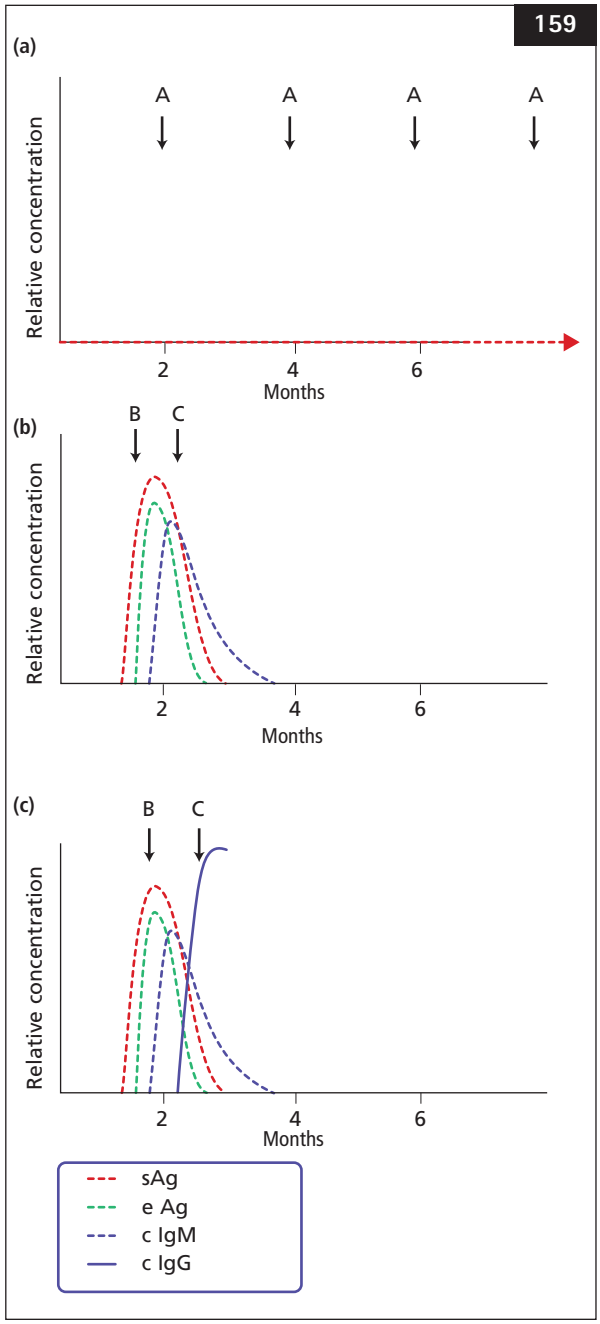
*The HBsAg test is done first on all specimens to determine if there is active infection present.

**These tests would not usually be done.

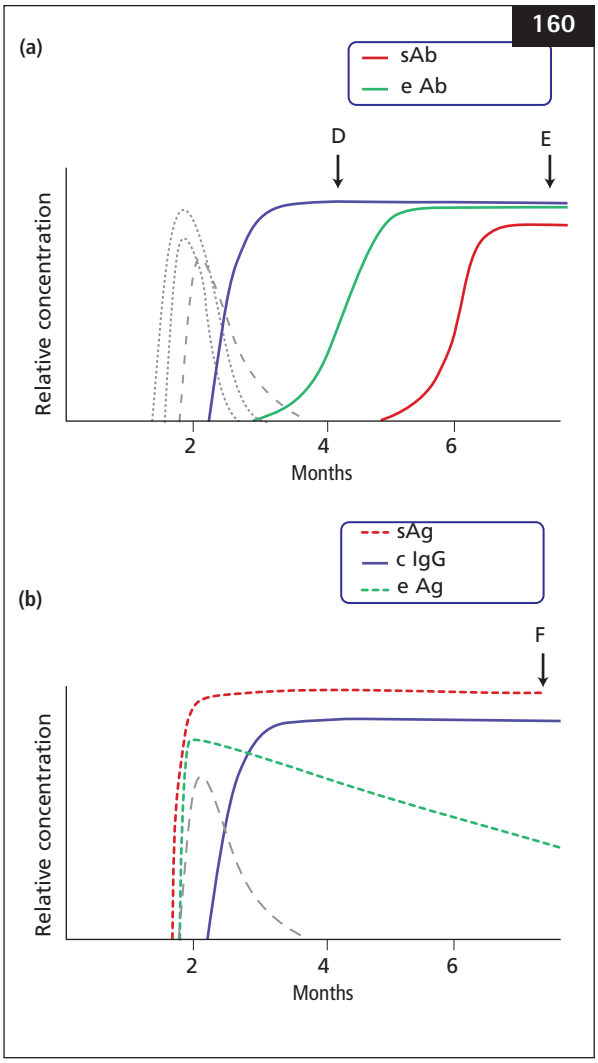
***HBsAg can be negative, as it is rapidly cleared by some individuals.

****The person who remains HBsAb negative after vaccination can either be a true nonresponder, the vaccine has not been delivered into muscle, or is chronically infected. After counselling, HBsAg and HBcAb tests are done to determine the status of the individual.

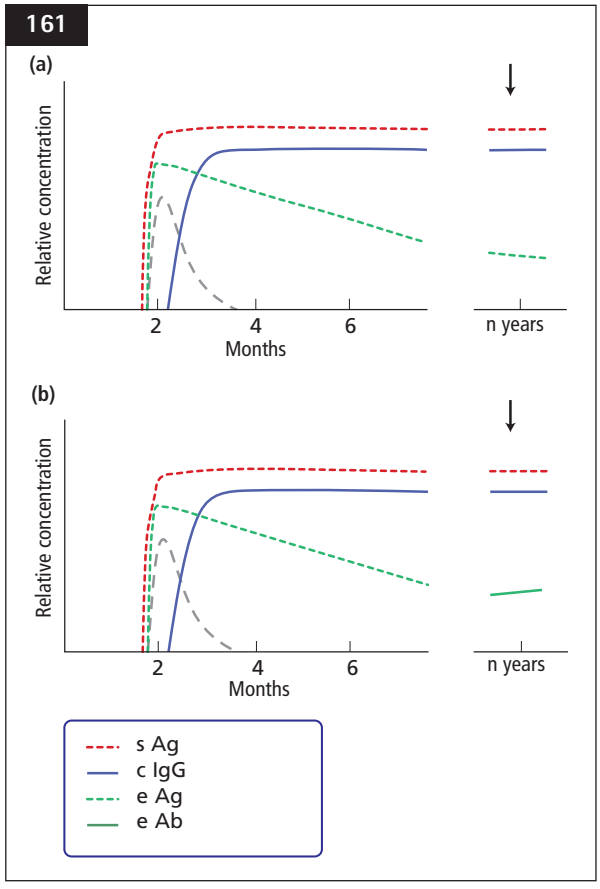
158 The HBV markers used to identify an acute infection, a recent infection, the development of natural immunity, chronic infection, and the response to vaccination. HBsAg is the first test that is done, as it is a sensitive and specific marker of active infection (replicating virus); the decision in the laboratory as to which further tests should be performed is determined by the clinical details on the request form. For cross reference, the relevant Figure and letter in that Figure should be noted.



159 The markers of acute HBV infection (**158** should be referred to). **(a)** The individual who has not been infected with HBV will be negative for all the markers at any time. Usually the HBsAg test only is done (A). **(b)** Although the diagnostic marker of acute infection is cIgM antibody, first virological marker is HBsAg (B), followed by HBeAg, and then appearance of HBcIgM antibodies (C). **(c)** HBcIgG antibodies then appear, which with the HBcIgM make up TOTAL HBcAb (C). The individual is considered infectious from when HBsAg appears, until the production of HBsAb some months later.



160 Following acute HBV infection, core IgG antibodies (HBcIgG) appear, and are life-long markers of past infection, but are NOT protective antibodies (D). There are two outcomes following acute infection, and this must be confirmed at about 6 months. **(a)** Natural immunity. After acute infection, there is loss of HBsAg, followed several months later by the appearance of surface antibodies (HBsAb), which confer natural immunity (E). The period between the loss of the HBsAg and appearance of HBsAb is the 'window' period (D). The patient should be considered infectious until HBsAb are detected. Antibodies (HBeAb) to HBeAg also appear. **(b)** Chronic carriage. There is continuing presence of HBsAg in the blood, reflecting ongoing virus replication in liver (F), which is confirmed by the presence of the HBeAg, a 'crude' marker of the degree of virus replication, and thus infectiousness. HBsAb, and thus natural immunity, do not appear. The patient being HBeAg positive is considered a 'high-risk' carrier here.



161 Chronic HBV infection. At 'n' years, a patient with abnormal LFT is screened for HBV, and is found to be HBsAg positive. **(a)** The markers are HBcIgG, HBsAg, and HBeAg showing chronic infection/carriage (HBsAg), and active virus replication (HBeAg). This is a 'high-risk' carrier. **(b)** At 'n' years for this patient, the markers are HBcIgG, HBsAg, and HBeAb. Most individuals mount an immune response to the HBeAg at some time, and HBeAb appear. Such individuals are generally considered to have lower levels of virus replication in the liver, and are classed 'low-risk' carriers.

Most HBV infections are asymptomatic, especially in children. The incubation period is about 60–90 days (range 45–180). Acute infection is diagnosed by the presence of IgM antibodies to the core antigen (HBcIgM) (**159**). HBsAg and HBeAg appear first and confirm virus replication. The patient is highly infectious at this time via blood and genital secretions, and should still be considered infectious until HBsAb are detected, showing that the infection has finally been cleared from the liver. The gap between the disappearance of HBsAg and appearance of HBsAb probably reflects the final stage in clearing the massive amounts of the surface antigen from the blood (**160**). The presence of HBsAb shows that the patient is now naturally immune to HBV infection. Protective HBsAb are also produced by vaccination.

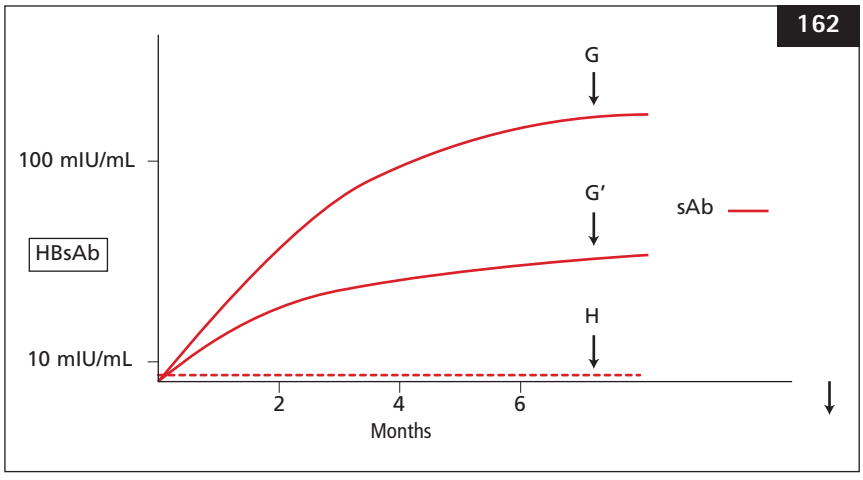
Follow-up of the patient 6 months after acute HBV infection is essential (**160**). A subset of patients cannot clear the virus and become chronic (HBsAg positive) carriers (**160**). The prevalence of chronic HBV carriage varies significantly, from 0.1 to 2.0% in the USA and Europe to over 8% in southeast Asia and China. The age of infection determines the likelihood of chronic carriage. If the infection occurs perinatally, the carriage rate is 90%, in the ages 1–5 years it is 10–20%, dropping to 5% in immunocompetent adults.[5] The presence of HBeAg shows ongoing high levels of virus replication, and 'high-risk' carrier status, whereas the presence of HBeAb usually shows viral replication has been 'reduced' to give the individual 'low-risk' status (**161**). All carriers should be referred to a gastroenterologist, as chronic active hepatitis, cirrhosis, and hepatocellular carcinoma are complications.

Immunization confers immunity in most vaccinated people (**162**). A negative response to vaccination may occur in the following situations:

1. Incorrect administration of vaccine. Vaccine must be given into muscle and in obese individuals, vaccine may be deposited in adipose tissue, where it does not stimulate an antibody response. A longer needle should always be used when vaccinating these patients.[6] A needle of at least 38 mm in length is recommended for women weighing over 90 kg.[7]
2. The patient is a true nonresponder to the vaccine, and will always be susceptible to the infection.
3. Patients who have had past infection. Patients should be tested for HBcAb and HBsAg; the presence of the antigen shows ongoing infection with native virus.

HCV

HCV is a member of the Flaviviridae, and has a single stranded (SS) RNA genome. It has two outer proteins, E1 and E2, and a core protein.[8] Antibodies produced following acute infection do not confer immunity. There are two reasons for this. First, there are (at least) six genotypes, and 25 subtypes of the virus. Second, a hypervariable region of the genome coding for 30 amino acids in the E2 protein, gives rise to continually changing amino acid sequences, and antigenic determinants.[8, 9] This enables the virus to 'escape' the immune system, as



162 Following a course of vaccination, the individual with HBsAb titres >100 mIU/mL is considered to have life-long immunity, but should receive a reinforcing dose of vaccine at 5 years. Those with antibody titres between 10 and 100 mIU/mL are also immune, but should be given a booster dose and the reinforcing dose at 5 years. Those with antibodies <10 mIU/mL will be in the following categories:

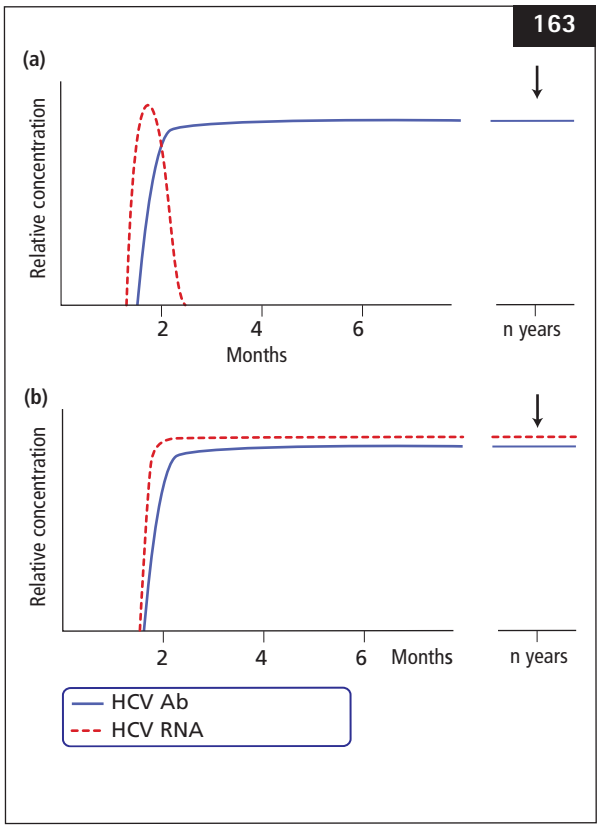
(1) Incorrect administration of vaccine. Vaccine must be given into muscle and in obese individuals vaccine may inadvertently go into adipose tissue at which site it does not produce/stimulate an antibody response. A longer needle should always be used when vaccinating these patients.[6, 7]

(2) The patient is a true nonresponder to the vaccine, and will always be susceptible to the infection.

(3) Patients who have had past infection. Patients should be tested for HBcAb and HBsAg; the presence of the antigen shows ongoing infection with native virus.

the heterogeneous antibodies produced against the changing E2 protein are not protective. The virus is blood-borne and IDU is a particular risk. Transmission is uncommon via sexual intercourse. Estimates of perinatal transmission vary between 0 to 4%.[10] Breast feeding is unlikely to be a risk.

Acute infection is asymptomatic and is seldom confirmed, but an incubation period of 60–90 days (range, 45–180) is recognized. There are two outcomes following infection, clearance of the virus, or chronic carriage. Overall, viraemia persists in 50–85% of infected individuals.[8] Most HCV infections are identified at screening, and RNA-PCR technology is essential. The presence of HCV antibodies in the absence of RNA shows that the person has cleared the virus; the presence of RNA confirms chronic carriage (**163**). All carriers should be referred to a gastroenterologist, as chronic active hepatitis, cirrhosis, and hepatocellular carcinoma are complications. HCV RNA obtained from the patient's blood is used to genotype the virus, as this determines those individuals who can be considered for treatment under the care of the hepatologist.



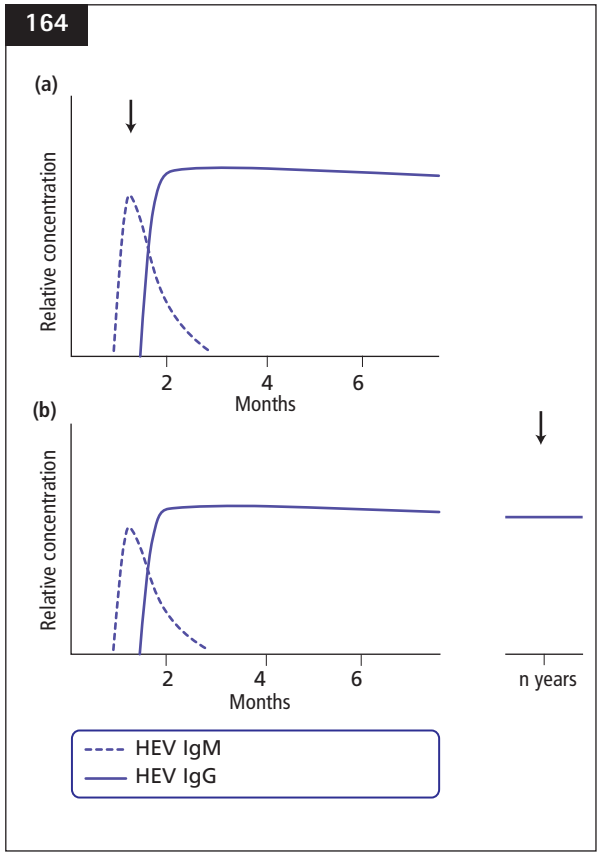
163 Noting that acute HCV is not usually diagnosed, infection is identified, when for example, a previous IDU asks at 'n' years if they have had HCV infection. **(a)** HCV antibodies detected and the PCR for HCV RNA is negative. (This should be confirmed by showing a second sample is also negative for HCV RNA.) HCV antibody positive and RNA negative confirm past infection, and excludes chronic carriage. The patient can be reassured, but still remains at risk of reinfection as HCV antibodies are heterogeneous and do not protect against further exposure to HCV. **(b)** HCV antibodies and HCV RNA detected. The patient is a chronic carrier of HCV.

HEV

HEV is a SS RNA virus, calicivirus-like, which is the single member of the Hepeviridae, and hepevirus genus; it is transmitted by the faecal–oral route.[11] The infection is often associated with travel to the Middle East and southeast Asia, but it is now considered that HEV infection in developed countries may be far more common than previously recognized. The source of these infections is not clear, but may have a porcine source.[11] Patients with unexplained hepatitis must be tested for HEV, irrespective of their age or travel history.

Most infections are asymptomatic, especially in children. The incubation period is about 45 days (range, 20–60 days), and acute infection diagnosed by the detection of HEV IgM antibodies, which may be present for 6–10 weeks after the acute infection. IgG antibodies are a marker of past infection (**164**). There are five genotypes of HEV, and one major antigenic determinant in immunity; the degree of long-term protection following infection is unclear.[11] Most clinical infections are mild, but severe infections occur in pregnancy, with a significant mortality rate of about 20%.[12] It is probably unwise for a pregnant person to travel to a known endemic region, unless this is really necessary.

164



164 The appearance of HEV IgM and IgG antibodies. (**a**) Patient with acute hepatitis. HEV IgM antibodies detected, evidence of acute infection. (**b**) Patient with jaundice. HEV IgM antibody negative, IgG antibody positive; previous HEV infection. The role of IgG antibodies in long-term immunity is unclear.

MANAGEMENT OF SHARPS/SPLASH INJURIES TO MEMBERS OF THE PUBLIC

All sharps/splash injuries should be considered medical emergencies, and the injured 'recipient' should be referred to the local accident and emergency department without delay. If the 'source' can be identified, risk assessed, and provide a blood sample for prompt BBV testing this helps the overall management, and determines the need for HBV immunoglobulin, HBV vaccination, and/or HIV antiviral prophylaxis in the recipient. Prompt advice should also be sought when a 'sharps' injury (e.g. clenched fist) occurs during assault, and both the aggressor and victim can be at risk of BBV infection. Not infrequently, in order to avoid the law, the aggressor presents several days later; immediate advice in this instance should be sought from the sexually transmitted disease (STD)/infectious disease physician. It is useful to determine any information about the 'source' in relation to HIV. Those considered to be in 'high-risk' groups include MSM, men who have sex with both men and women, commercial sex workers, injection drug users, people with history of incarceration, people who are from a country where the seroprevalence is 1% or greater, or a person who has a sexual partner of one of these groups.[13]

An example of a sharps injury which can be dealt with in primary care is the parent reporting that the child has picked up a needle in the park and pricked herself/himself, often many hours after the event; the parents are often concerned about HIV in particular. The needle is likely to have been discarded for some time and any small volume of blood in the bore of the needle will probably have dried. There is no convincing evidence of transmission of HBV in these situations, by far the most contagious of these BBV. Thus, based on our knowledge of these BBV, the risk of transmission of all three viruses, and HIV in particular should be considered low. The parent can be reassured, and if this is not possible, the STD physician should be contacted. (Note that the accepted transmission rate of HBV, HCV, and HIV in a 'significant' injury in the health-care setting from an infected individual is 30%, 3%, and 0.3%).

In addition, the following is done:

1. Collect baseline blood from the child for long-term (2 year) storage. The specimen should be sent to the medical microbiology/virology department with the clinical details clearly stated on the request form as 'serum save; recipient of sharps injury'.
2. Despite the risk of HBV transmission being very low, it is reasonable to initiate a rapid course of the HBV vaccine; the doses are given at 0, 1, and 2 months. (A booster dose at 12 months only needs to be given if there is an ongoing risk of exposure).
3. The child and family can then be referred to the paediatrician for counselling, reassurance, and follow-up blood tests.

SUMMARY AND KEY POINTS

In summary, the following points should be noted:

- The practice/clinic should establish guidelines for both clinical and nursing staff to use so that there are set criteria, centred around Quick Action Guides and the critical steps of **144**.
- These should be used regularly as a training tool to give guidance on when and how to collect specimens, and how the laboratory report should be interpreted.
- Key to the whole process is provision of the full clinical details on the request form so that the laboratory can determine which serology tests need to be done.
- Regular training programmes must emphasize the situations that are urgent requiring prompt communication with the laboratory. Exposure to VZV in pregnancy is the classic example where the process not infrequently goes wrong because the urgency of the situation is not recognized at the practice/clinic.

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10

Infections in Pregnancy

- Introduction
- Role of the antenatal clinic
- Organisms to consider in pregnancy; prepregnancy counselling, and the role of screening
- Screening for HBV, HIV, rubella, and syphilis
- Exposure to a rash-like illness during pregnancy
- The pregnant patient with a rash
- Group B streptococcus (GBS)
- Urinary tract infections in pregnancy
- Vaginal discharges and STD
- Other infections in pregnancy
- Vaccinations in pregnancy
- Summary and key points

INTRODUCTION

The subject of this chapter is usually dealt with by the community and hospital midwife and the obstetrician, with the appropriate involvement of the medical microbiologist/virologist. The primary care physician has a key role as well, and the most important in managing the urgent situation, such as the example given in **165**, which is then the basis for the Quick Action Guide. Practices should use these for training purposes, and have protocols in place for the prompt management of these situations. Important topics are:

- Management of the pregnant patient exposed to a rash-like illness.[1]
- The management of the pregnant patient who develops a rash.[1]
- Screening for asymptomatic bacteriuria in pregnancy.
- Management of urinary tract infection (UTI) in pregnancy.
- Group B streptococcus in pregnancy.
- Antenatal screening for blood-borne virus (BBV).

ROLE OF THE ANTENATAL CLINIC

Key to management of a number of infections in pregnancy is the first visit to the antenatal clinic (ANC), or the primary care midwife at about 12 weeks. The patient will be counselled about the routine testing done for hepatitis B (HBV), human immunodeficiency virus (HIV), rubella, and syphilis. If there is a risk of hepatitis C virus (HCV), for example the pregnant woman with a history of intravenous drug use (IDU), this should also be screened for, although the risk to the fetus and newborn is low.[2] Patients who are found to be positive for any of the above infections (apart from rubella) will need to be managed appropriately during the pregnancy. Where there is an ongoing risk, and of HBV and HIV in particular, screening should be repeated during the remainder of the pregnancy if the patient cannot reduce the risk. Immunization against HBV should be considered in pregnancy where a significant ongoing risk is identified, and the patient shows no serological markers of prior infection. Results of all these tests must be clearly recorded in the patient's notes. If the patient confirms a history of chickenpox, or herpes zoster, this information should also be documented. For those with no history, advice should be given to seek medical help as soon as possible after any exposure. All patients should be told that if they are in contact with an individual who has a rash illness, or they develop a rash illness themselves, they should seek medical advice as soon as possible. Those with a rash should be asked to contact the practice/clinic or ANC in advance so that they can be seen in a separate area so as not to put others at risk.

165 Managing chickenpox in pregnancy, the importance of immediate communication with the laboratory. The steps in the process can be divided into seven critical steps. (See Chapter 1, 1).

Exposure of the pregnant individual to a rash-like illness should be considered a medical emergency. With chickenpox, the minimum incubation period is 10 days, and where indicated, VZIG has to be given *within* 10 days. Note that an infected individual is infectious for up to 2 days before the rash appears.

In this case, the pregnant patient was exposed to VZV on the previous Thursday, and if infected she would be 9 days into the incubation period by the Saturday morning, so action must be completed immediately. This situation is a not uncommon, where the urgency is not recognized in primary care at critical step 1, when the laboratory should have been contacted immediately. The patient should be made aware that she must be contactable, and if necessary her telephone number given to the medical microbiologist.

Critical step 3 is also breached, as the clinical details give no information about the date of the exposure. This then entails considerable work by the microbiologist on the Saturday morning to make the situation 'safe', all of which could have been addressed on the Friday.

Storing and transport of specimens for serology

Clotted blood should be collected in the appropriate tube. It is always helpful if a full container is collected, so that sufficient serum can be 'tapped off'. Where a delay in transport is acceptable (routine specimens), these can be refrigerated in the designated refrigerator.

165

CRITICAL STEP 1:
Is collection of a specimen indicated?

The community midwife sees a woman who is 16/40 weeks pregnant on Friday afternoon. The patient says she was at a children's party the previous Thursday. She was told yesterday that one of the children she had contact with came out in a chickenpox rash the next day. The patient has not had chickenpox before.

CRITICAL STEP 2:
Obtain a good quality specimen.

Specimen of clotted blood is collected.

CRITICAL STEP 3:

Record the full patient and clinical details on the request form. Where necessary, record the specific test request.

The clinical details put on the request form are: '16/40 weeks pregnant, chicken pox contact'.

CRITICAL STEP 4:

How is the specimen stored and what is the frequency of transport to the laboratory?

Specimen delivered by routine transport.

CRITICAL STEP 5:

What is the quality of the laboratory process, including turnaround times?

On Saturday morning, the laboratory staff identify the specimen in the routine transport from primary care. They note the request, and the specimen is processed promptly.

CRITICAL STEP 6:

Is immediate or routine reporting of this result required by the laboratory?

The result must be communicated NOW by the microbiologist to the primary care physician.

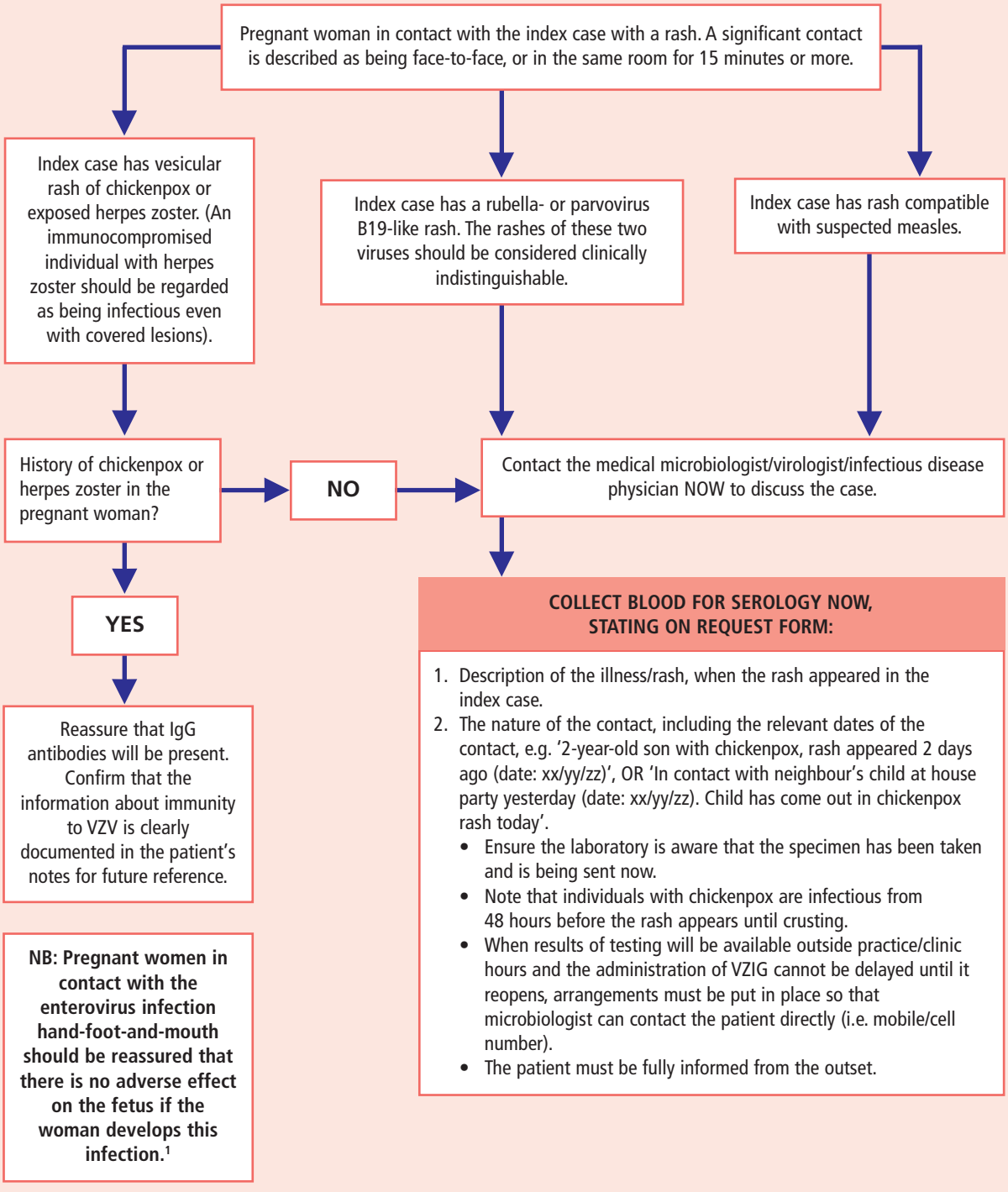
CRITICAL STEP 7:
How is the laboratory report interpreted?

Report on AB, 16 weeks pregnant: VZV IgG antibodies NOT detected. Susceptible to chickenpox.

The primary care practice/clinic is closed, and the patient has to be contacted by the microbiologist using her home telephone number available on the hospital record. The patient gives the information about the day of exposure, which is now 9 days ago. The microbiologist organizes for the patient to have VZIG administered, ensuring that she does not come into contact with susceptible patients or staff. If the patient returns to ANC within the 10–21 day incubation period, she must be nursed in a side room by staff who know they are immune to VZV.

Quick Action Guide

The steps to be used in the management of a pregnant patient exposed to an index case with a rash-like illness. Adapted in part from Morgan-Capner *et al*.[1] Reproduced with permission of the UK Health Protection Agency.


Pregnant woman in contact with the index case with a rash. A significant contact is described as being face-to-face, or in the same room for 15 minutes or more.
Index case has vesicular rash of chickenpox or exposed herpes zoster. (An immunocompromised individual with herpes zoster should be regarded as being infectious even with covered lesions).
Index case has a rubella- or parvovirus B19-like rash. The rashes of these two viruses should be considered clinically indistinguishable.
Index case has rash compatible with suspected measles.
History of chickenpox or herpes zoster in the pregnant woman?
NO
Contact the medical microbiologist/virologist/infectious disease physician NOW to discuss the case.
YES
Reassure that IgG antibodies will be present. Confirm that the information about immunity to VZV is clearly documented in the patient's notes for future reference.
COLLECT BLOOD FOR SEROLOGY NOW, STATING ON REQUEST FORM:
1. Description of the illness/rash, when the rash appeared in the index case.
2. The nature of the contact, including the relevant dates of the contact, e.g. '2-year-old son with chickenpox, rash appeared 2 days ago (date: xx/yy/zz)', OR 'In contact with neighbour's child at house party yesterday (date: xx/yy/zz). Child has come out in chickenpox rash today'.
• Ensure the laboratory is aware that the specimen has been taken and is being sent now.
• Note that individuals with chickenpox are infectious from 48 hours before the rash appears until crusting.
• When results of testing will be available outside practice/clinic hours and the administration of VZIG cannot be delayed until it reopens, arrangements must be put in place so that microbiologist can contact the patient directly (i.e. mobile/cell number).
• The patient must be fully informed from the outset.
NB: Pregnant women in contact with the enterovirus infection hand-foot-and-mouth should be reassured that there is no adverse effect on the fetus if the woman develops this infection.[1]

ORGANISMS TO CONSIDER IN PREGNANCY; PREPREGNANCY COUNSELLING, AND THE ROLE OF SCREENING

While the majority of pregnancies proceed without complication, there is a risk that an infection prior to conception, during gestation, or around the time of birth can affect the mother, developing fetus, or newborn. It is for this reason that a patient who is contemplating pregnancy for the first time may ask about infections in pregnancy, which infections she is likely to be immune to, and the steps that can be taken to reduce risk. A list of organisms and conditions to consider in pregnancy is given in **166**.

While rubella infection is prevented by routine childhood vaccination, routine vaccination for varicella zoster virus (VZV) is not currently available. However, if the patient has a definite history of chickenpox, she will have natural immunity. If a woman works or lives with cats, and is concerned about a risk of toxoplasmosis, then serology can be done; careful food and hand hygiene should be reinforced to minimize further risk.

At the first antenatal visit the patient will be counselled to have blood taken for HBV, rubella, syphilis, and HIV testing. The laboratory should store an aliquot of this 'booking blood', as it can provide a useful comparative baseline for serological investigation of an infection, such as CMV, later in pregnancy. In addition, mid-stream urine (MSU) is collected for examination to exclude asymptomatic bacteriuria (Chapter 3). It is important at this time to explain to the patient the reason for these tests, and also risks of other infections. UTI and sexually transmitted infection (STI) in pregnancy should be discussed, and both must be promptly diagnosed and treated.

166

Organism	Risk period for fetus/newborn	Consequences Fetus/child	Mother
Group B streptococcus	Preterm labour, PROM	Neonatal sepsis/meningitis	(Wound infection)
*Treponema pallidum**	Gestation	Congenital syphilis	Syphilis
HBV*	Mainly in perinatal period	Chronic HBV infection	Cirrhosis, HCC
HIV*	Mainly from 28 weeks onwards	Chronic HIV infection	Untreated HIV
Rubella*	First trimester	Death, serious defects	Acute rubella
Parvovirus B19	First 20 weeks	Death, hydrops foetalis	Acute parvovirus B19
VZV	First 20 weeks and neonatal period	Limb hypoplasia (<20 weeks), neonatal death, herpes zoster	Chicken pox and VZV pneumonia
Measles	Duration of gestation	Intrauterine death	Measles and complications of preterm delivery
CMV	Primary infection (esp. first 20/40)	Congenital CMV	Often asymptomatic
Herpes simplex 2/1	Last trimester, neonatal period	Disseminated neonatal herpes	Genital herpes
Toxoplasmosis	Gestation	Congenital toxoplasmosis	Toxoplasmosis
Bacterial vaginosis	Last trimester	Preterm labour	Bacterial vaginosis
UTI (asymptomatic)*	Gestation	IUGR	UTI (pyelonephritis), gram-negative sepsis

Organisms/conditions marked (*) should be routinely screened for at the first antenatal visit.

166 A list of infections/organisms to consider in pregnancy that can affect either the foetus, neonate, or mother. (IUGR: intrauterine growth retardation).

SCREENING FOR HBV, HIV, RUBELLA, AND SYPHILIS

Antenatal screening for HBV, HIV, rubella, and syphilis usually gives the result shown in **167**, and the patient can be reassured. However, any mother who may be at continued risk of acquisition of one of these organisms should be counselled to have further tests later in pregnancy, and informed of the ways that risks can be reduced. This advice would apply, for example, to the expectant mother whose lifestyle may increase the risk of HIV, or she is from a population group where there is a higher incidence of HIV.

The woman who is rubella IgG antibody negative is susceptible to rubella infection, and must be told that she needs to seek prompt medical advice if she comes into contact with an individual who has a rash illness. She also requires rubella

167

Name: JB
Age: 28 years

Clinical details: Pregnant; first ANC visit screen at 12/40 weeks. Routine antenatal screen.

(Tests requested: HBsAg, HIV antigen/antibody, rubella IgG antibody, treponemal antibodies).

RESULT

HBV surface antigen NEGATIVE
HIV 1 and 2 antibody and antigen NEGATIVE
Rubella IgG POSITIVE; consider rubella immune
Treponema pallidum antibody NEGATIVE

167 The usual result that is obtained on blood taken at the 12 week antenatal screening visit, shows the patient is not infected with HBV, HIV, or *Treponema pallidum*, and is immune to rubella infection. The clinical details direct the laboratory staff to do these four serology tests.

168

Organism	Relevance	Marker	Risk assessment
HBV	Maternal chronic carriage*	HBsAg positive	HBeAg +/HBeAb – = 'high-risk' carrier** HBeAg –/HBeAb + = 'low-risk' carrier**
HIV	Maternal infection	HIV Ag/Ab positive	Increasing risk of transmission to fetus, especially from 28 weeks, at delivery, and with breast feeding.
Rubella	Maternal susceptibility	Rubella IgG negative	Exposure to rubella in first 14 weeks carries a significant risk to fetus.
Treponema	Maternal chronic/latent infection	Treponema TPPA/IgG positive VDRL positive, treponemal IgM+	Exclude congenital infection at birth, and monitor for loss of maternal antibodies during first 12 months of life.

*There is also a high risk of transmission during acute HBV infection in the mother.
**See Chapter 9.

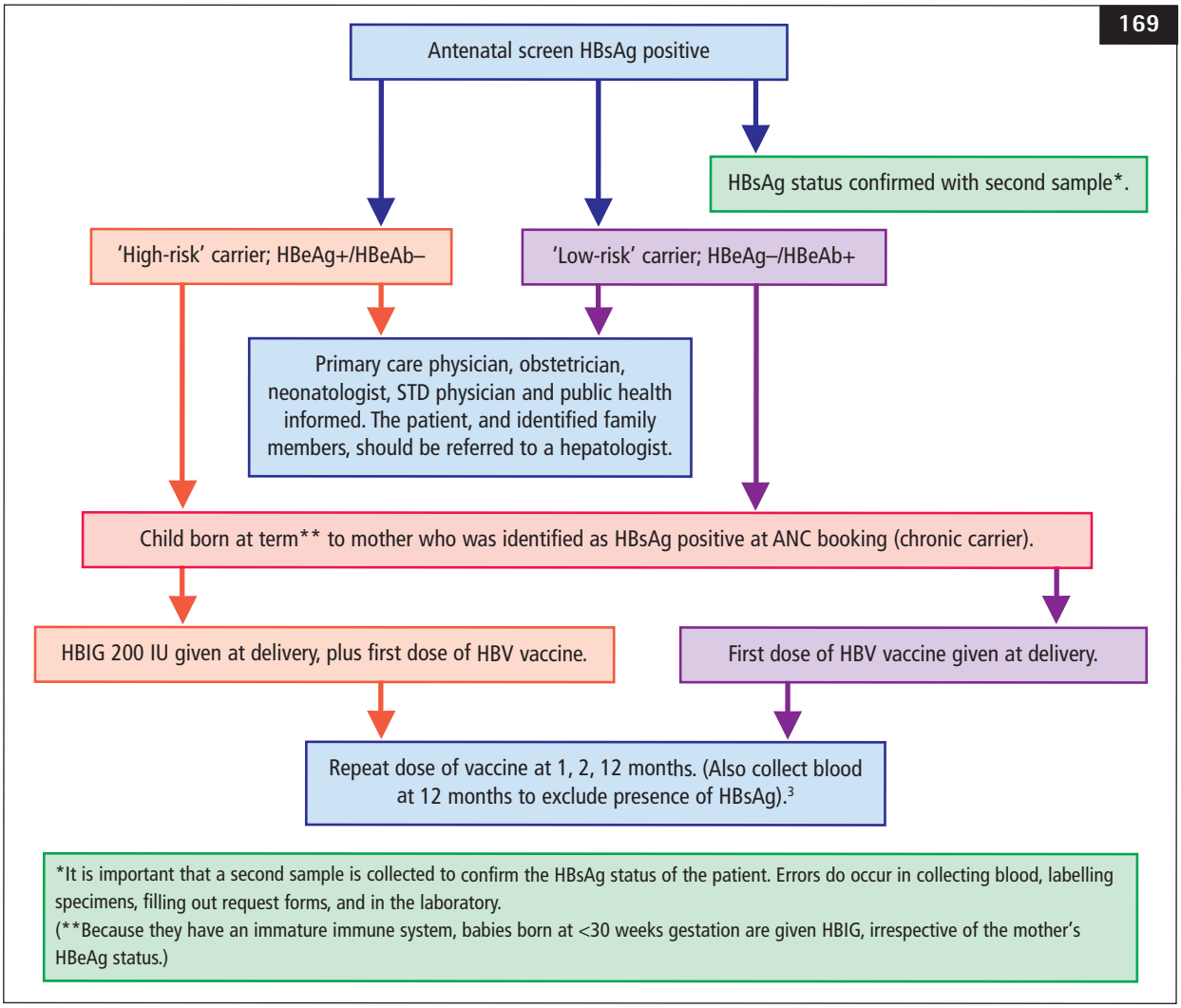
168 The markers determining the risk of congenital/perinatal transmission of HBV, HIV, rubella, and syphilis.

vaccination after the baby is born. The relevance of the infection status of the pregnant woman in relation to HBV, HIV, rubella, and syphilis is summarized in **168**.

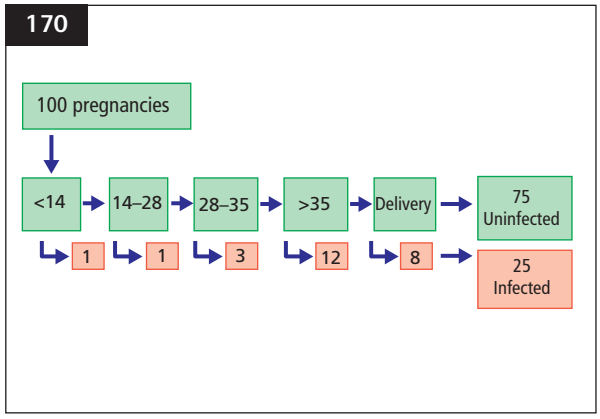
When a woman is identified as being infected with HBV, HIV, or syphilis in pregnancy, it is important to collect a second blood sample to confirm the status. Errors do occasionally occur in specimen collection, labelling blood tubes, filling out the request form, and in the laboratory. A second blood sample which confirms the first result essentially rules out any error.

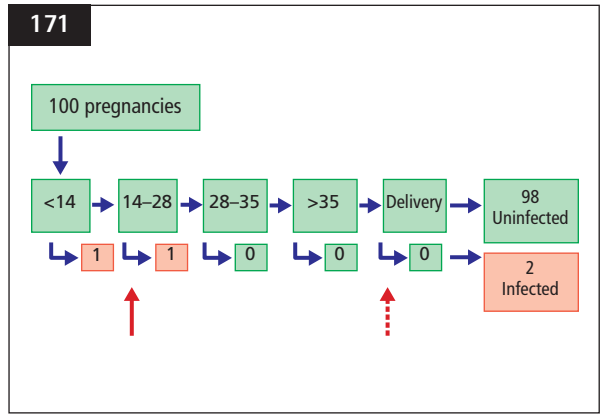
HBV

The mother who is positive for HBV surface antigen (HBsAg) is infectious, and as outlined in Chapter 9, further antigen and antibody markers are tested to confirm chronic (or acute) HBV infection. In chronic infection, the HBV 'e' antigen and antibody (HBeAg/HBeAb) markers are used to determine 'high-risk' or 'low-risk' status. With HBV, most transmission events occur during the passage of the child through the birth canal. An outline of the process involved in managing a pregnant woman who is HBsAg positive is shown in **169**. Following notification, family contacts would be screened and managed by public health using set protocols.[3]


169
Antenatal screen HBsAg positive
HBsAg status confirmed with second sample*.
'High-risk' carrier; HBeAg+/HBeAb–
'Low-risk' carrier; HBeAg–/HBeAb+
Primary care physician, obstetrician, neonatologist, STD physician and public health informed. The patient, and identified family members, should be referred to a hepatologist.
Child born at term** to mother who was identified as HBsAg positive at ANC booking (chronic carrier).
HBIG 200 IU given at delivery, plus first dose of HBV vaccine.
First dose of HBV vaccine given at delivery.
Repeat dose of vaccine at 1, 2, 12 months. (Also collect blood at 12 months to exclude presence of HBsAg).[3]
*It is important that a second sample is collected to confirm the HBsAg status of the patient. Errors do occur in collecting blood, labelling specimens, filling out request forms, and in the laboratory.
(**Because they have an immature immune system, babies born at <30 weeks gestation are given HBIG, irrespective of the mother's HBeAg status.)

169 The outline of the process involved once a pregnant woman is identified as a HBV carrier in pregnancy.





170, 171 (170) Without antiviral intervention, transmission of HIV during pregnancy, and at birth, means that 25/100 babies will be infected. (Breast feeding for 6 months will infect a further 6/100 babies.) **(171)** With antiviral intervention starting in the mother (red arrow) and newborn (dotted arrow), and as necessary Caesarean section, transmission falls to about 2/100 babies. (Adapted from Kourtis *et al.*[4] With permission from Elsevier Publishing.)

HIV

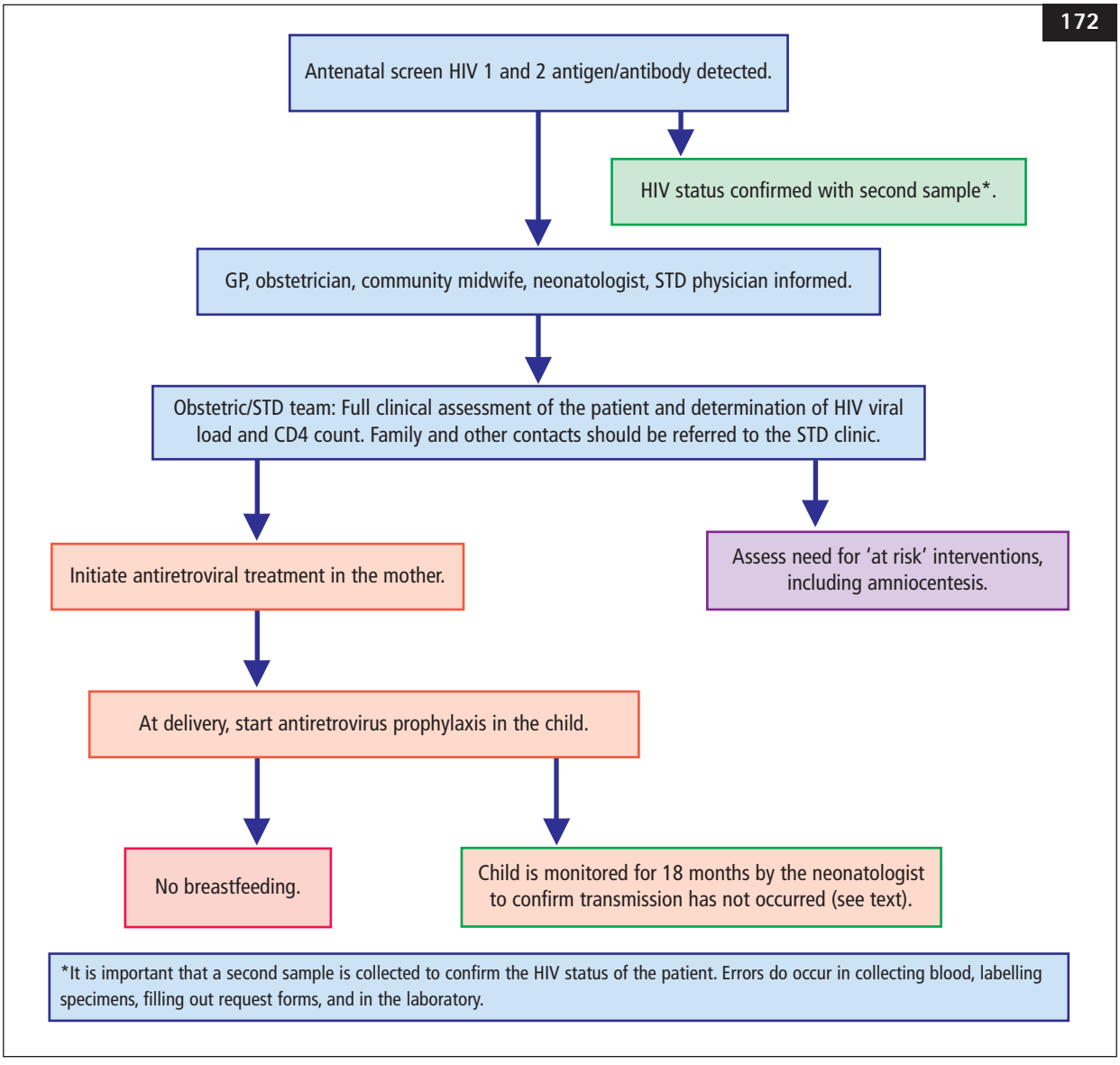
The chances of the fetus/newborn acquiring HIV during various stages in pregnancy and perinatally, and the effect of antiviral therapy in reducing this is shown in **170, 171.**[4] The effect of antivirals is so dramatic that it underlines the importance of being proactive about recommending the HIV test. Early diagnosis also enables the obstetrician to review the need for interventions such as amniocentesis, which can increase the risk of transmission. An outline of the process in managing HIV infection in pregnancy is shown in **172.**

After birth, it is essential to confirm that the child has not acquired HIV from the mother, and to do this both molecular (polymerase chain reaction [PCR]) and serology tests are done. After delivery, and then at 6, 12, and 24 weeks, the key test is examining samples of deoxyribonucleic acid (DNA) extracted from peripheral white blood cells (WBCs) of the child for HIV proviral DNA; a negative result shows the virus is absent. The essential positive control in the test is detection of HIV proviral DNA in a sample of the mother's blood examined in parallel, which uses the same 'primers' in the PCR amplification process.

The final test to confirm that transmission has not taken place is done at 18 months of age. A blood specimen must be negative for HIV ribonucleic acid (RNA) by PCR, and for antibodies to HIV (by this time maternal antibodies acquired by passive immunity during gestation will have disappeared).

Rubella

Management of exposure to a rash-like illness or suspected rubella infection in the rubella immune or susceptible individual in pregnancy is covered in detail in the next section.


172
Antenatal screen HIV 1 and 2 antigen/antibody detected.
HIV status confirmed with second sample*.
GP, obstetrician, community midwife, neonatologist, STD physician informed.
Obstetric/STD team: Full clinical assessment of the patient and determination of HIV viral load and CD4 count. Family and other contacts should be referred to the STD clinic.
Initiate antiretroviral treatment in the mother.
Assess need for 'at risk' interventions, including amniocentesis.
At delivery, start antiretrovirus prophylaxis in the child.
No breastfeeding.
Child is monitored for 18 months by the neonatologist to confirm transmission has not occurred (see text).
*It is important that a second sample is collected to confirm the HIV status of the patient. Errors do occur in collecting blood, labelling specimens, filling out request forms, and in the laboratory.

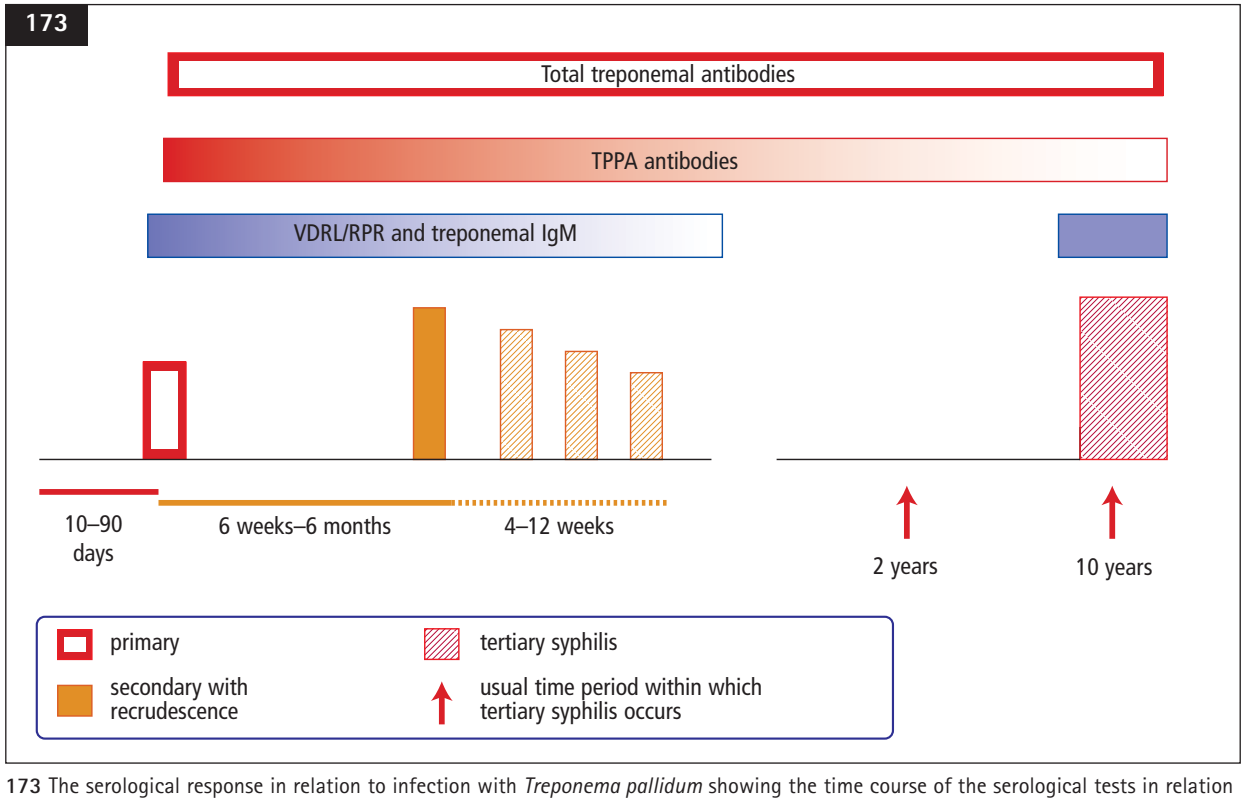
172 The outline of the process once the pregnant woman has been identified as HIV infected in pregnancy.

Syphilis

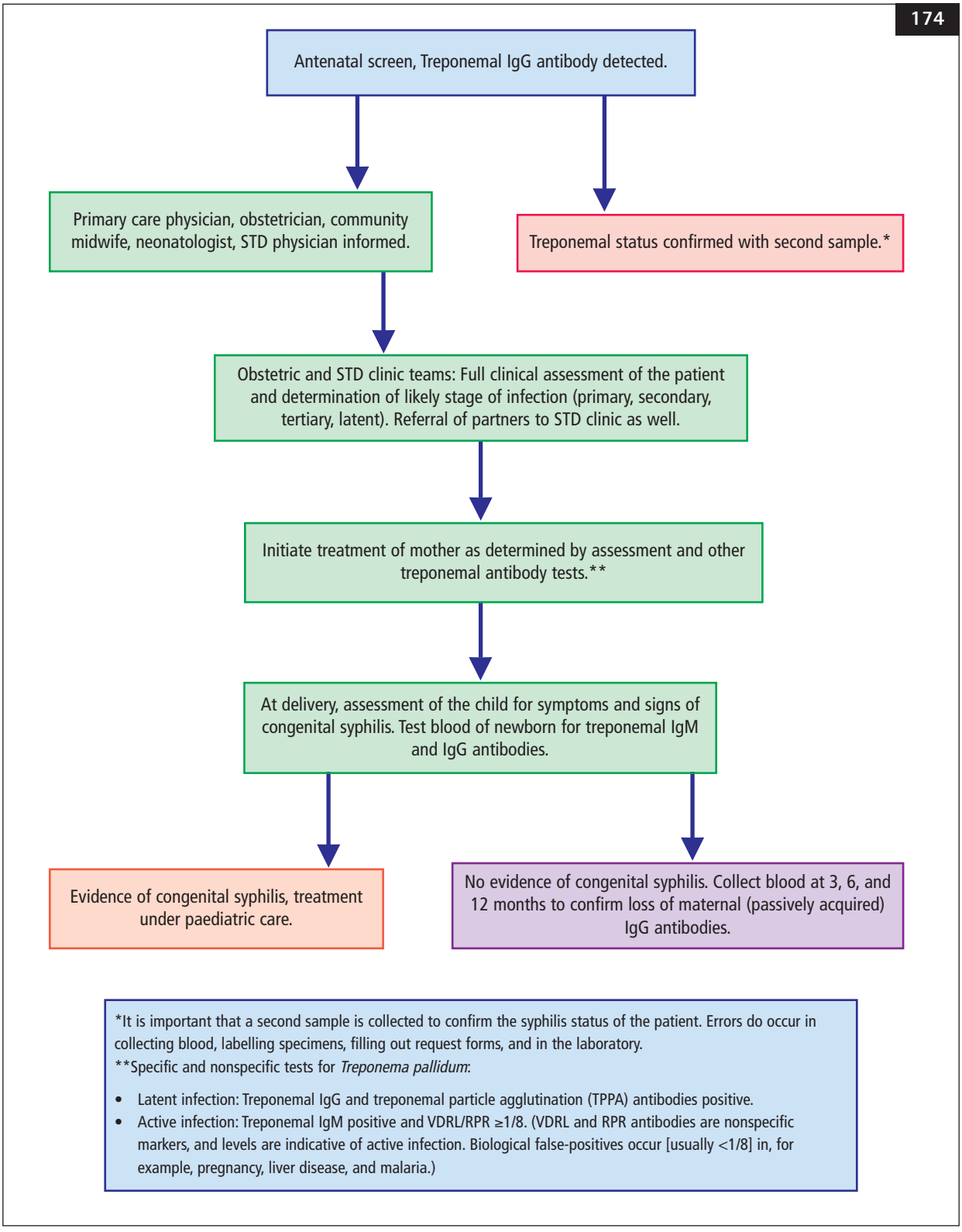
The natural history of syphilis infection and the antibody responses are shown in **173**. Syphilis is a complicated infection, with the individual being infectious during the various milestones of the disease. Although transmission to the fetus can occur at any stage of maternal disease, it is more likely to occur in primary or secondary disease.[5] Unless there is documented evidence that the mother with positive serology has had appropriate treatment, treatment would usually be indicated; these patients would usually be under the care of the sexually transmitted disease (STD) physician.

The presence of IgG antibodies to *Treponema pallidum* shows that the woman has been infected with the bacterium at some stage in her life. Treponemal IgM and venereal disease research laboratory/rapid plasma reagin (VDRL/RPR) antibodies determine whether or not there is active disease. VDRL/RPR IgG antibodies are nonspecific markers of active disease. They are also found in conditions other than syphilis, including malaria, hepatitis, and pregnancy itself. Titres in these conditions are generally low (<1/8), whereas in active syphilis, VDRL titres are usually in excess of 1/8.

The process of managing the treponemal antibody-positive patient in pregnancy is shown in **174**. Following careful clinical assessment of the newborn after birth to exclude congenital infection, blood is tested for treponemal IgM and IgG antibody to confirm there is no serological evidence of infection. Protocols may vary, but the child should be tested at 3, 6, and 12 months to confirm that there is loss of passively acquired maternal IgG antibody.



173 The serological response in relation to infection with *Treponema pallidum* showing the time course of the serological tests in relation to the stages of the disease. After an incubation period of 10–90 days, the primary chancre appears, and 6 weeks to 6 months after resolution, secondary syphilis appears. Recrudescence can occur, followed by early latent (<2 years) and late latent disease (2–10 years). Tertiary syphilis is the last stage. Congenital infection can occur at any stage of the maternal disease.


174
Antenatal screen, Treponemal IgG antibody detected.
Primary care physician, obstetrician, community midwife, neonatologist, STD physician informed.
Treponemal status confirmed with second sample.*
Obstetric and STD clinic teams: Full clinical assessment of the patient and determination of likely stage of infection (primary, secondary, tertiary, latent). Referral of partners to STD clinic as well.
Initiate treatment of mother as determined by assessment and other treponemal antibody tests.**
At delivery, assessment of the child for symptoms and signs of congenital syphilis. Test blood of newborn for treponemal IgM and IgG antibodies.
Evidence of congenital syphilis, treatment under paediatric care.
No evidence of congenital syphilis. Collect blood at 3, 6, and 12 months to confirm loss of maternal (passively acquired) IgG antibodies.
*It is important that a second sample is collected to confirm the syphilis status of the patient. Errors do occur in collecting blood, labelling specimens, filling out request forms, and in the laboratory.
**Specific and nonspecific tests for Treponema pallidum:
• Latent infection: Treponemal IgG and treponemal particle agglutination (TPPA) antibodies positive.
• Active infection: Treponemal IgM positive and VDRL/RPR ≥1/8. (VDRL and RPR antibodies are nonspecific markers, and levels are indicative of active infection. Biological false-positives occur [usually <1/8] in, for example, pregnancy, liver disease, and malaria.)

174 Outline of the process once the patient has been identified as treponemal antibody positive in pregnancy.

175

	Rubella	Parvovirus B19	VZV
% susceptible young adults	1–2	40–50	10
Risk of transmission from close contact	High (90%)	Medium (50%)	High (70–90%)
Risk of transmission to fetus	<11 weeks: 90% 11–16 weeks: 55% >16 weeks: 45%	<4 weeks: 0% 5–16 weeks: 15% >16 weeks: 25–70%	<28 weeks: 5–10% 28–36 weeks: 25% >36 weeks: 50%
Risk of adverse outcome to fetus	<11 weeks: 90% 11–16 weeks: 20% 16–20 weeks: minimal risk of deafness only >20 weeks, no increased risk	<20 weeks: 9% excess foetal loss. 3% hydrops, of which 50% die. >20 weeks no increased risk	CVS*: <13 weeks: 1% 13–20 weeks: 2%. –4 to +2 days perinatal: 20% neonatal varicella
Risk to mother	Arthritis	Arthritis	Pneumonitis, with fatality rate of 0.1% infections in pregnancy
Interventions	Termination	Hydrops; intrauterine transfusion reduces odds of death to 0.14	VZIG**; mother/neonate or aciclovir within 24 hr of rash for mother, or for exposed neonate
Incubation period	14–21 days	13–18 days	10–21 days
Infectivity in relation to rash	–7 to +10 days	–10 to 0 days	–2 days to cropping ceases and lesions crust

*Congenital varicella syndrome (CVS) can manifest as limb hypoplasia and herpes zoster.

**VZIG must be given to the susceptible woman within 10 days of exposure. VZIG attenuates the infection in the mother, and the neonate when it needs to be given after birth.

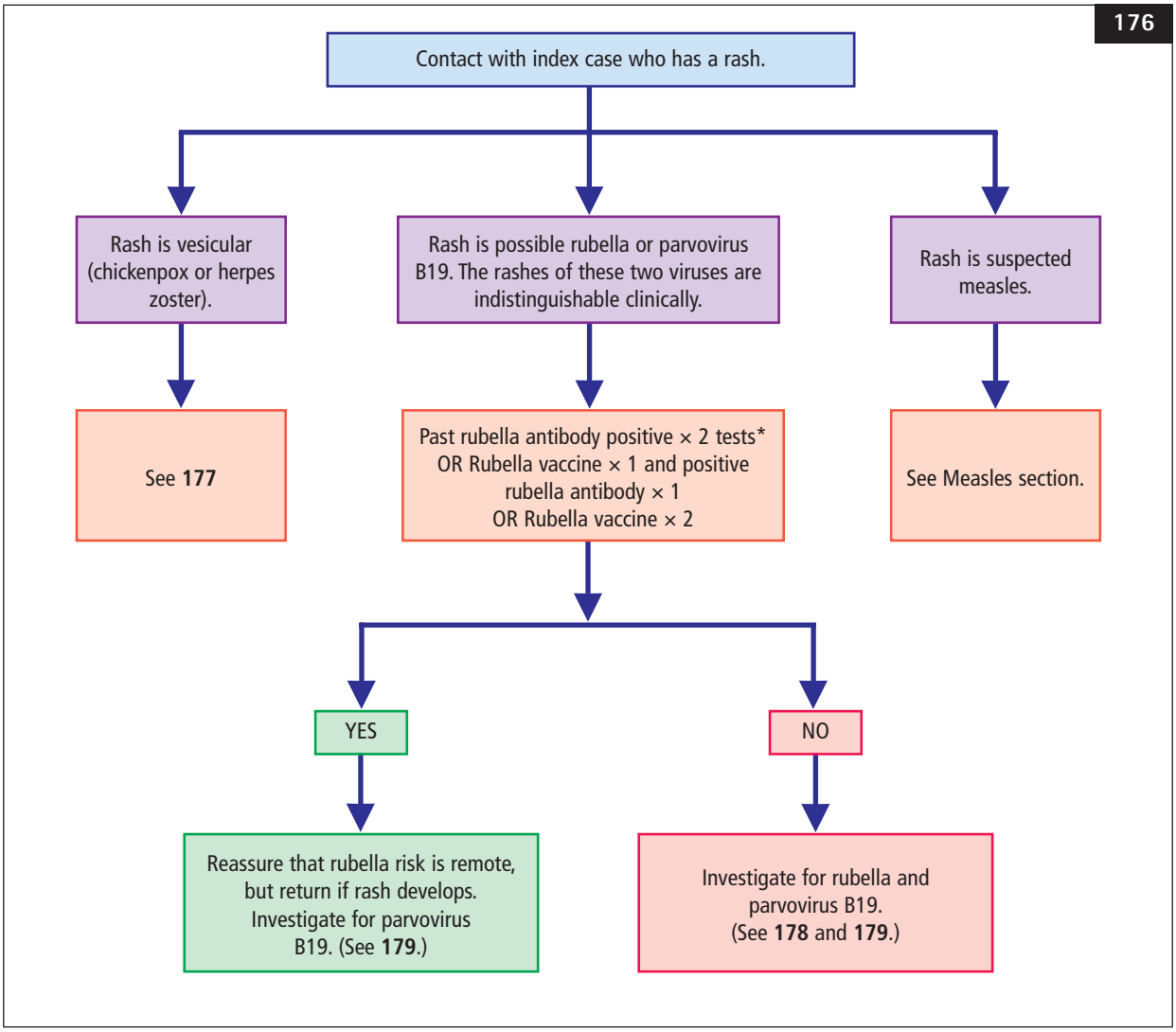
175 Important features of rubella, parvovirus B19, and VZV infection in pregnancy. (From Morgan-Capner *et al.*[1] Reproduced with permission of the UK Health Protection Agency.)

EXPOSURE TO A RASH-LIKE ILLNESS DURING PREGNANCY

Rash illnesses to consider in pregnancy include chickenpox, rubella, parvovirus B19, and measles. The rashes associated with rubella and parvovirus B19 are clinically indistinguishable and serological investigations must be done for both these viruses. Rashes can also occur with enterovirus infections, including hand-foot-and-mouth disease (see Quick Action Guide, and the Exanthems section).[1]

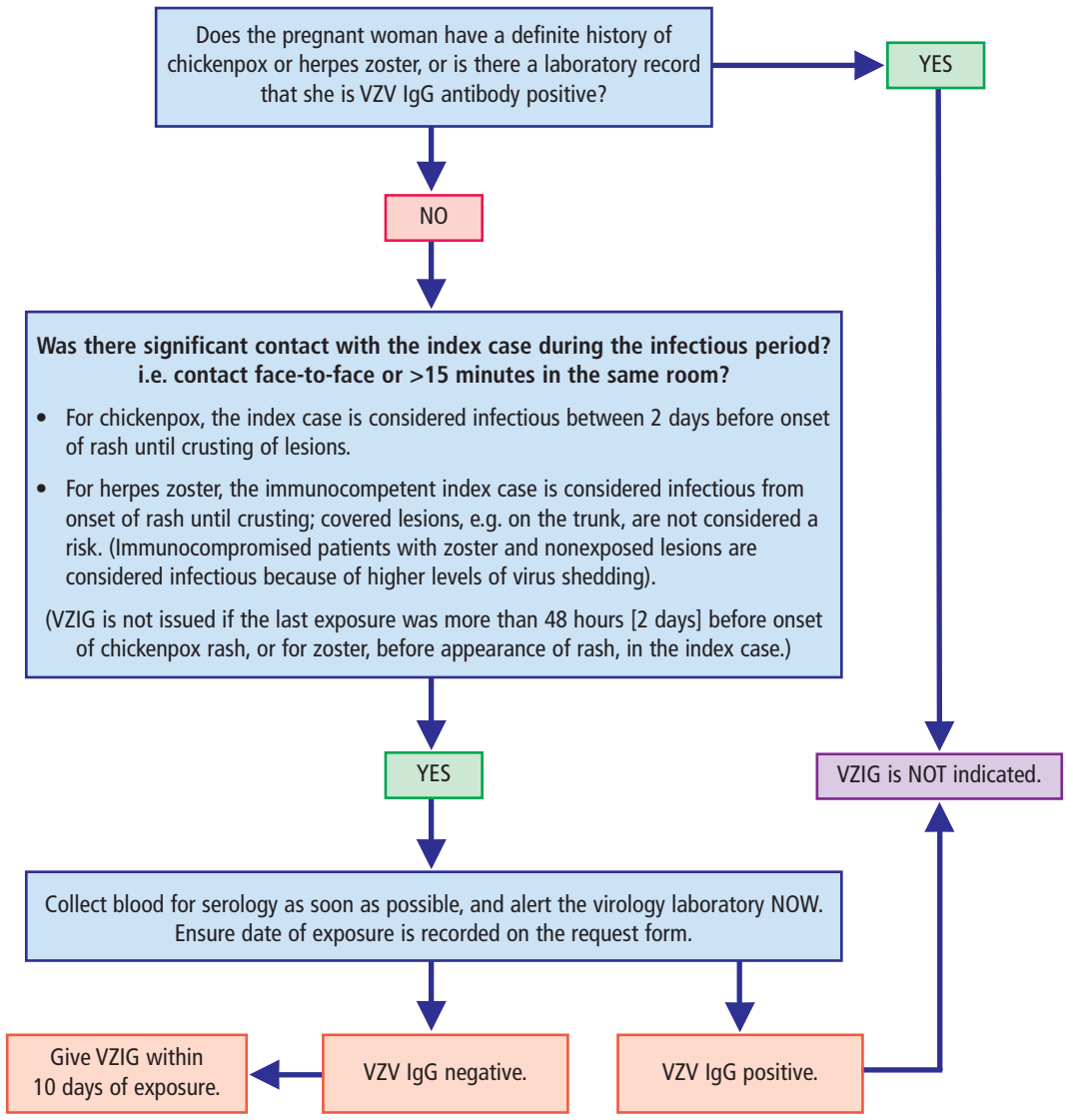
Some relevant features of rubella, parvovirus B19, and VZV infection in pregnancy are shown in **175**.[1]

Figure **176** shows the algorithm for the initial management of the patient. While exposure to VZV in pregnancy can be managed by the primary care physician and medical microbiologist/virologist, confirmed infection with any of these viruses requires referral to the obstetrician.


176
Contact with index case who has a rash.
Rash is vesicular (chickenpox or herpes zoster).
Rash is possible rubella or parvovirus B19. The rashes of these two viruses are indistinguishable clinically.
Rash is suspected measles.
See 177
Past rubella antibody positive × 2 tests*
OR Rubella vaccine × 1 and positive rubella antibody × 1
OR Rubella vaccine × 2
See Measles section.
YES
NO
Reassure that rubella risk is remote, but return if rash develops. Investigate for parvovirus B19. (See 179.)
Investigate for rubella and parvovirus B19. (See 178 and 179.)

176 An outline of the initial management strategy used by the medical microbiologist/virologist for the pregnant woman exposed to a rash illness. If the susceptible pregnant woman reports exposure to VZV 8–10 days ago, she may be in the prodromal period, and thus potentially infectious to others; do not send to ANC without prior arrangement. Similarly, the patient must not be allowed to wait in the waiting room. Other viral infections associated with a rash are those caused by enteroviruses, where infection in pregnancy is not associated with congenital abnormalities. *Two rubella antibody positive tests on the patient are to rule out any errors that may have occurred at the time of specimen collection, labelling the request form, or in the laboratory. (From Morgan-Capner *et al.*[1] Reproduced with permission of the UK Health Protection Agency.)

177

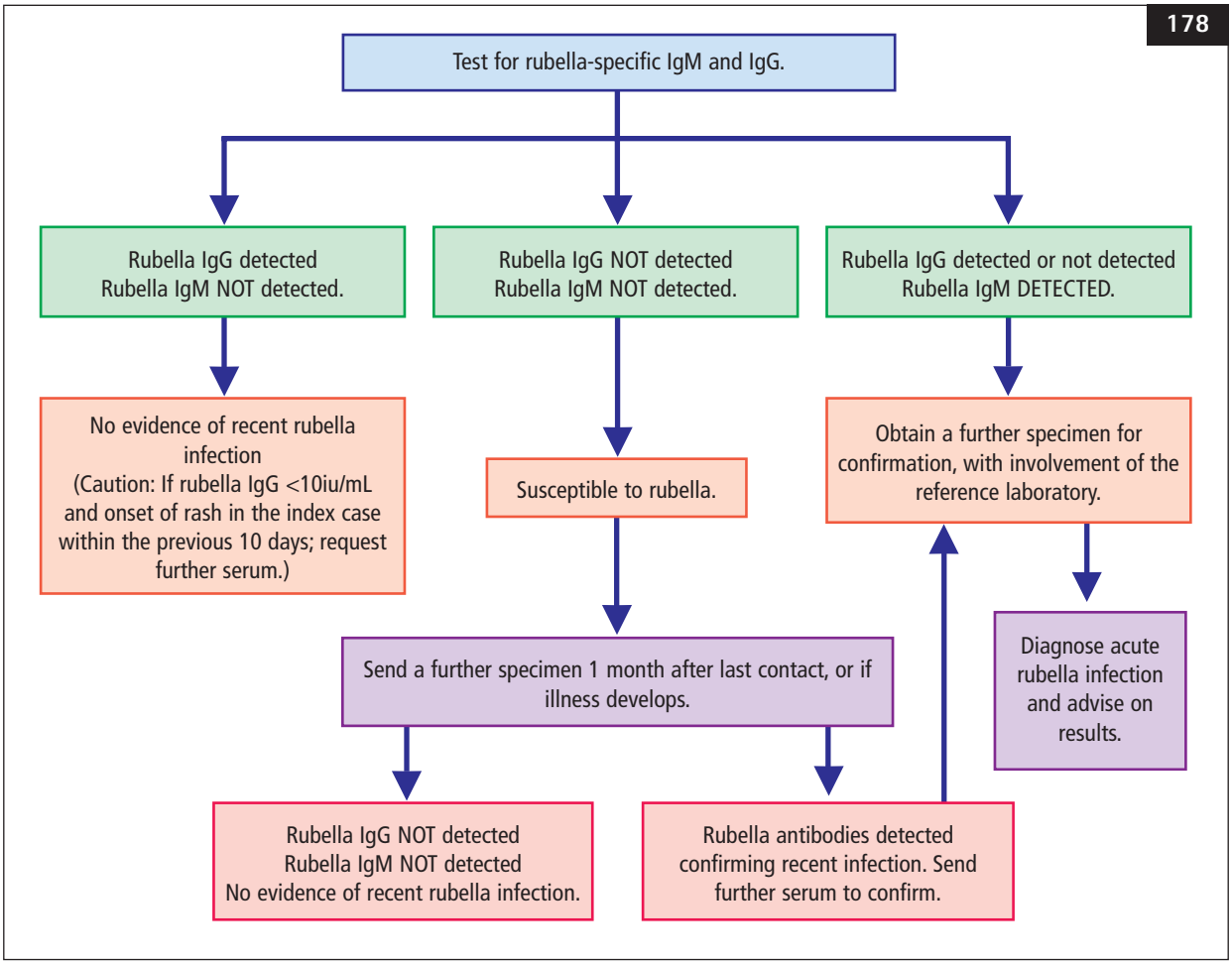

Does the pregnant woman have a definite history of chickenpox or herpes zoster, or is there a laboratory record that she is VZV IgG antibody positive?
YES
NO
Was there significant contact with the index case during the infectious period? i.e. contact face-to-face or >15 minutes in the same room?
• For chickenpox, the index case is considered infectious between 2 days before onset of rash until crusting of lesions.
• For herpes zoster, the immunocompetent index case is considered infectious from onset of rash until crusting; covered lesions, e.g. on the trunk, are not considered a risk. (Immunocompromised patients with zoster and nonexposed lesions are considered infectious because of higher levels of virus shedding).
(VZIG is not issued if the last exposure was more than 48 hours [2 days] before onset of chickenpox rash, or for zoster, before appearance of rash, in the index case.)
YES
VZIG is NOT indicated.
Collect blood for serology as soon as possible, and alert the virology laboratory NOW. Ensure date of exposure is recorded on the request form.
Give VZIG within 10 days of exposure.
VZV IgG negative.
VZV IgG positive.

177 The algorithm that can be used to determine if VZIG is needed following exposure of a pregnant woman to the index case with chickenpox or exposed herpes zoster, or an immunocompromised individual with zoster.[1, 3] Most problems in primary care arise due to a delay in the patient presenting after exposure, and staff not recognizing the urgency of the situation. The medical microbiologist/virologist would be involved in management of these situations. See the 'Green Book' for further details.[3] (Note that VZIG does not necessarily prevent infection, but modifies it to a milder illness, lessening the risk to the fetus and mother.)

VZV

The algorithm to use following exposure to chickenpox or herpes zoster is shown in **177**. Also see Chapter 9, **147**.

The nature of the exposure is important. The minimum contact time is considered to be 15 minutes in the same room, or face to face. With herpes zoster, covered lesions do not pose a risk unless the index case is immunosuppressed, where viral shedding from skin lesions is significantly greater. Adult chickenpox can progress to a life-threatening pneumonitis, and smoking is a risk factor. These cases on occasion result in admission to critical care, emphasizing the need to assess carefully the pregnant woman with acute VZV infection. If a susceptible patient presents more than


178
Test for rubella-specific IgM and IgG.
Rubella IgG detected
Rubella IgM NOT detected.
Rubella IgG NOT detected
Rubella IgM NOT detected.
Rubella IgG detected or not detected
Rubella IgM DETECTED.
No evidence of recent rubella infection
(Caution: If rubella IgG <10iu/mL and onset of rash in the index case within the previous 10 days; request further serum.)
Susceptible to rubella.
Obtain a further specimen for confirmation, with involvement of the reference laboratory.
Send a further specimen 1 month after last contact, or if illness develops.
Diagnose acute rubella infection and advise on results.
Rubella IgG NOT detected
Rubella IgM NOT detected
No evidence of recent rubella infection.
Rubella antibodies detected confirming recent infection. Send further serum to confirm.

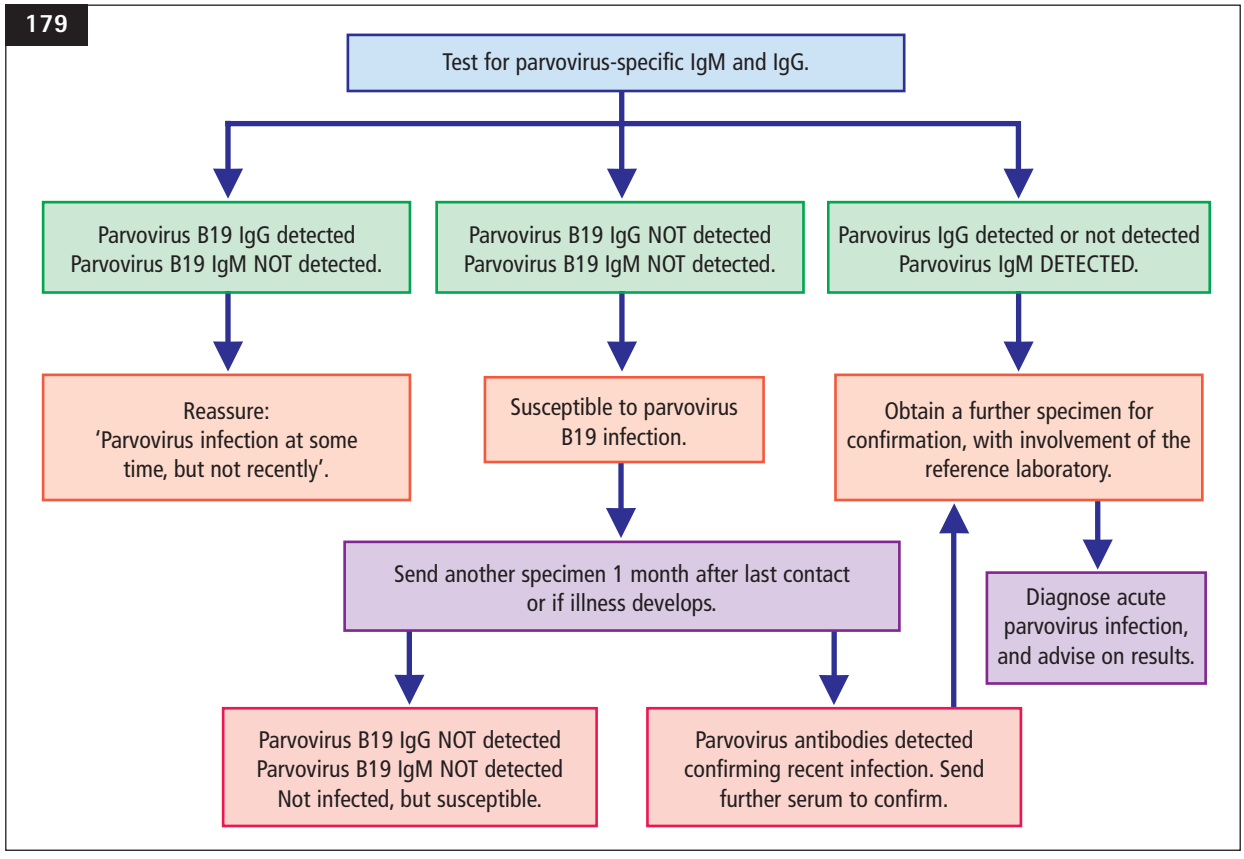
178 Investigation of rubella in a pregnant woman with significant exposure to the index case with a rash illness. (From Morgan-Capner *et al.*[1] Reproduced with permission of the UK Health Protection Agency.)

10 days after a contact, she should be prescribed aciclovir, and advised to start this immediately when the rash appears (aciclovir for maximum benefit should be taken within 24 hours of appearance of rash). This prescription circumvents the problem of medical access over weekends.

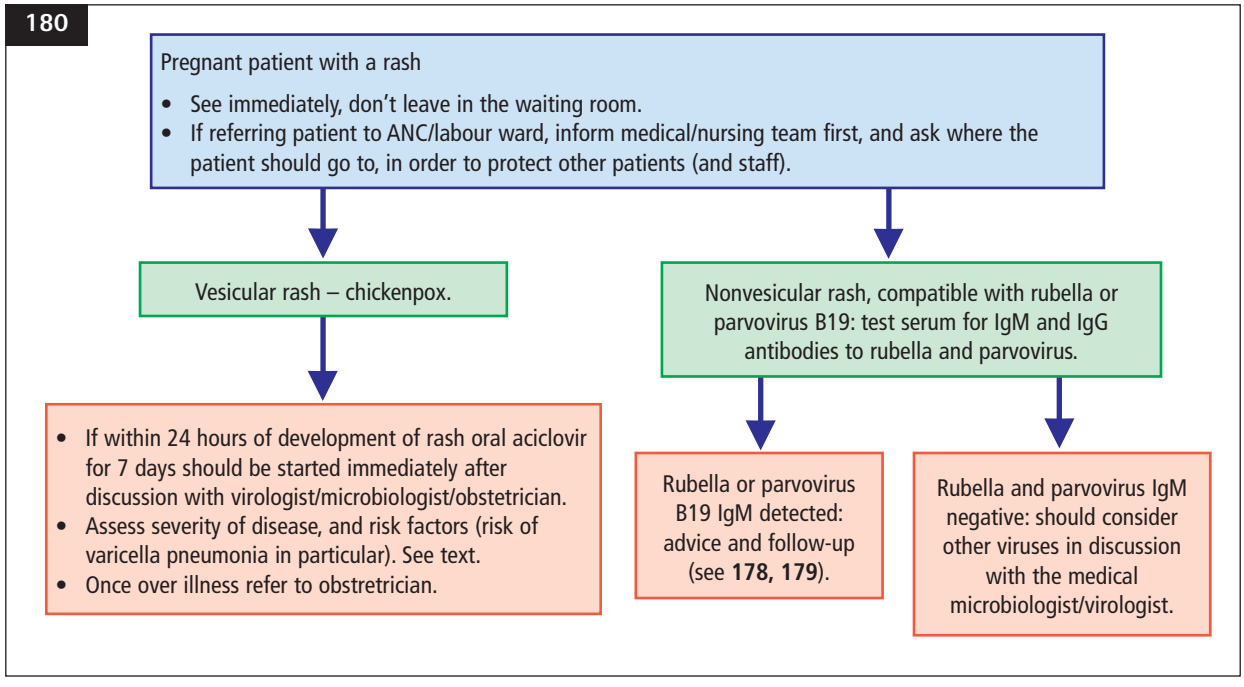
If a mother develops chickenpox in pregnancy, there is a risk to the fetus of limb hypoplasia, microcephaly, growth retardation, and skin scarring. The incidence of congenital varicella syndrome ranges from 1–2% in the first 20 weeks, after which the risk is substantially lower. There is a significant risk of neonatal mortality if the mother develops chickenpox 7 days before, to 7 days after delivery (or if the neonate whose mother is seronegative is exposed to VZV from any source within the first 7 days of life). These situations are usually managed by the obstetrician and neonatal teams, with the input of the medical microbiologist/virologist. Details are given in the 'Green Book'.[3]

Rubella and parvovirus

The algorithm for the investigation of exposure to rubella or parvovirus in a pregnant woman with significant exposure to a rash illness is shown in **178** and **179**.


179
Test for parvovirus-specific IgM and IgG.
Parvovirus B19 IgG detected
Parvovirus B19 IgM NOT detected.
Parvovirus B19 IgG NOT detected
Parvovirus B19 IgM NOT detected.
Parvovirus IgG detected or not detected
Parvovirus IgM DETECTED.
Reassure:
'Parvovirus infection at some time, but not recently'.
Susceptible to parvovirus B19 infection.
Obtain a further specimen for confirmation, with involvement of the reference laboratory.
Send another specimen 1 month after last contact or if illness develops.
Diagnose acute parvovirus infection, and advise on results.
Parvovirus B19 IgG NOT detected
Parvovirus B19 IgM NOT detected
Not infected, but susceptible.
Parvovirus antibodies detected confirming recent infection. Send further serum to confirm.

179 Investigation of parvovirus B19 in a pregnant woman with significant exposure to the index case with a rash illness. (From Morgan-Capner *et al.*[1] Reproduced with permission of the UK Health Protection Agency.)


180
Pregnant patient with a rash
• See immediately, don't leave in the waiting room.
• If referring patient to ANC/labour ward, inform medical/nursing team first, and ask where the patient should go to, in order to protect other patients (and staff).
Vesicular rash – chickenpox.
Nonvesicular rash, compatible with rubella or parvovirus B19: test serum for IgM and IgG antibodies to rubella and parvovirus.
• If within 24 hours of development of rash oral aciclovir for 7 days should be started immediately after discussion with virologist/microbiologist/obstetrician.
• Assess severity of disease, and risk factors (risk of varicella pneumonia in particular). See text.
• Once over illness refer to obstretrician.
Rubella or parvovirus B19 IgM detected: advice and follow-up (see 178, 179).
Rubella and parvovirus IgM negative: should consider other viruses in discussion with the medical microbiologist/virologist.

180 An outline of the process that should be followed in managing the pregnant patient with a rash. (From Morgan-Capner *et al.*[1] Reproduced with permission of the UK Health Protection Agency.)

Measles
If the woman has documented evidence of two doses of measles vaccine, she should be considered immune, and reassured. If this evidence is not available, serum should be tested promptly. If measles-specific IgG antibody is detected within 6 days of exposure, then further action is not necessary. If IgG antibody is not detected, human normal immunoglobulin (HNIG) is given, within 6 days of exposure.[1, 6]

THE PREGNANT PATIENT WITH A RASH
It is important that the risk of transmission of any infection to other pregnant individuals is minimized, and prompt infection control is in place. Staff should always be aware that a patient with a rash must not sit in the waiting area, but must be seen immediately. Similarly, if the patient has to be referred to ANC or the labour ward, staff there must be informed in advance, so that the patient can be seen in a separate area when she arrives. This is outlined in **180**.

VZV
The risks to the mother of serious illness with chickenpox, particularly in the third trimester should be recognized. Aciclovir should be prescribed for 7 days and started within 24 hours of the rash appearing. If the infection is uncomplicated, the woman can be reassured and sent home with daily review. Indications for hospitalization are shown below:

Absolute indicators
- Chest symptoms (this is usually a late sign as due to significant pulmonary reserve. By the time the patient develops symptoms the disease is advanced).
- Neurological symptoms other than headache.
- Bleeding rash.
- Dense rash/numerous mucosal lesions.
- Retrosternal chest pain.
- Illness longer than 6 days.
- Significant immunosuppression.

Contributory factors
- Pregnancy approaching term.
- Bad obstetric history.
- Smoker.
- Chronic lung disease.
- Poor social circumstances.
- The primary care physician is unable to monitor patient at least daily.

Rubella and parvovirus B19
The presence of a rubella/parvovirus-like rash requires collection of blood and testing for the IgM and IgG antibody of the two viruses. If IgM antibody is present, or there is seroconversion, referral to the obstetrician is done, taking into account gestational age.

GROUP B STREPTOCOCCUS (GBS)
Patients may ask about GBS at antenatal visits. It is important that health professionals appreciate that GBS is a member of the bowel flora, from where it can become part of the 'normal flora' of the perineum and vagina. Colonization rates in pregnant and nonpregnant women range from 10 to 40%.[7] The principal reservoir is the rectum.[8] GBS can cause asymptomatic bacteriuria, which can be an indication of heavy vaginal colonization. The rate of vertical transmission at the time of birth is about 50%.[9] Factors that increase the risk of invasive disease in the newborn include delivery at less than 37 weeks, amniotic membrane rupture ≥18 hours and maternal fever ≥38°C.[7]

Countries vary in their approach to GBS in pregnancy, and the management process at delivery; local guidelines must be used. In the USA, the CDC Guidelines recommend that pregnant women are screened with vaginal and rectal swabs between 35 and 37 weeks gestation, unless they are already considered 'GBS positive' with a previous infant having invasive GBS disease, or have had a GBS bacteriuria in this pregnancy.[10]

Indications for prophylactic antibiotics for the mother during labour are then as follows:
- Previous infant with invasive GBS disease.
- GBS bacteriuria in the current pregnancy.
- Positive GBS screening culture in the current pregnancy.
- GBS status unknown, and any of the following:
  - Delivery <37 weeks.
  - Amniotic membrane rupture ≥18 hours.
  - Intrapartum temperature ≥38°C.

In primary care the key points are:
- Carriage of GBS in nonpregnant and pregnant women is common.
- Antibiotics do not eradicate GBS vaginal carriage (and are therefore not indicated), as recolonization will occur with organisms from the rectum. The role of antibiotics is at the time of labour.
- GBS is not a cause of a simple vaginal discharge.

URINARY TRACT INFECTIONS IN PREGNANCY

Although the role of bacteriuria in pregnancy and prematurity is not well defined, the relationship between asymptomatic bacteriuria and acute pyelonephritis is undisputed. The prevalence of asymptomatic bacteriuria in early pregnancy is about 5%, and if untreated about 20–40% of patients will develop acute pyelonephritis later in pregnancy. This compares with about 1% of patients who do not have bacteriuria early in pregnancy who later develop pyelonephritis.[11]

For this reason, screening at the first antenatal visit is important, and ideally screening should also be done in the third trimester. A clean-catch MSU should be obtained, and irrespective of the white cell count (WCC), the presence of a pure growth of an organism of $>10^7$ cfu/L is significant. As a single specimen is not diagnostic of asymptomatic bacteriuria, a second MSU should be collected to confirm the presence of the same organism, based on its identity and antibiotic susceptibility profile. It is so important that advice about correct specimen collection is given (see Chapter 3). Antibiotics should be prescribed for 7 days. One to two weeks after completion of treatment, a further MSU should be collected to confirm eradication of the infection. At each subsequent ANC visit, a MSU should be collected to confirm that the bacteriuria has not recurred.

Treatment is based on the susceptibility profile of the organism. In addition to amoxicillin, trimethoprim, and nitrofurantoin are considered acceptable to use in pregnancy (see Chapter 11).

VAGINAL DISCHARGES AND STD

Bacterial vaginosis, candidiasis, trichomoniasis, gonorrhoea, and chlamydia should be diagnosed by the appropriate method and treated. It is recognized that bacterial vaginosis and gonococcus are associated with preterm delivery and premature labour, and neonatal chlamydia and gonococcal infections are important entities (see Chapter 4).

Treatment of bacterial vaginosis, candidiasis, and trichomoniasis can be achieved by using relevant topical agents. Oral metronidazole can be prescribed for bacterial vaginosis and trichomonas, but high-dose regimes should not be used (see Chapter 11). Uncomplicated gonococcal infection can be treated by a single 500 mg intramuscular dose of ceftriaxone. Chlamydia is treated with erythromycin. The usual regime is 500 mg q6h for 7 days, but for patients who cannot tolerate the gastrointestinal side-effects, 250 mg q6h for 14 days is an option. A test of cure should be done at 5–6 weeks (see Chapter 4).

Patients with a likely STI must be referred to the STD clinic, where screening for STI will be done. This is particularly important where there is potential ongoing exposure to the BBV and syphilis.

OTHER INFECTIONS IN PREGNANCY

Cytomegalovirus

Cytomegalovirus (CMV) is the leading cause of congenital infection, with a prevalence of about 1%. Intrauterine infection rates are highest in primary infection (up to 50%), and although a risk is at any stage, it is highest when primary infection occurs in the first half of pregnancy. Clinically significant infections occur most often in infants born of primiparous mother with a primary infection. The severity of congenital infection ranges from neonatal jaundice, hepatosplenomegaly, peticheal rash, multi-organ involvement, microcephaly, chorioretinitis, and cerebral calcifications through to children who have normal cognitive and intellectual development, but of whom 8–15% have sensineural hearing loss. Most infections acquired perinatally are asymptomatic, and usually cause no long-term problems, although subtle hearing loss may be detected in later childhood.

The patient with a febrile illness, and altered liver function tests should be investigated. It is important for the medical microbiologist/virologist to have access to the 'booking blood' collected for HBV, HIV, rubella, and syphilis screening, as this can be used to determine if there has been seroconversion, and likely primary CMV infection. The management of these patients is then the domain of the obstetrician and medical virologist.

Neonatal herpes

Neonatal herpes has a high morbidity and mortality. Preconception, a woman may be concerned that either she or her partner has oral or genital herpes and may ask about the risk herpes poses to the fetus and newborn. General advice on avoiding oral sex, the use of condoms outside the 'conceptual' period, and the use of suppressive antiviral treatment for the partner can be discussed. The Herpes Virus Association provides helpful advice for individuals, and can be contacted at: info@herpes.org.uk or www.herpes.org.uk. Genital herpes in the female during pregnancy is categorized as first episode or recurrent. The trimester that a first episode occurs, the use of suppressive aciclovir, and delivery by Caesarean section are examples of key aspects of obstetric management. All women should undergo careful vulval inspection at the onset of labour to check for clinical signs of herpes infection. If a women develops primary infection or lesions near term she should be referred promptly to the obstetrician.

Toxoplasmosis

In the USA and Europe, only about 10–20% of cases of toxoplasmosis in the immunocompetent are symptomatic.[12] However, about 3–7% of clinically significant lymphadenopathy is likely to be due to acute toxoplasmosis.[13] Infectious mononucleosis-like illness with fever, malaise, night sweats, sore throat, maculopapular rash, and hepatosplenomegaly lasting for several weeks or months may occur on occasion[13] (see Chapter 9, appendix; Epstein–Barr virus).

Screening for toxoplasmosis may be requested by a woman from a country where screening in pregnancy is routine. This should be done as epidemiology may vary between countries. Screening for toxoplasmosis is not routinely performed in countries where the risk of infection in pregnancy is considered low, such as the UK. When toxoplasmosis infection is considered in pregnancy, serum is screened for total toxoplasma antibodies. If these are present, the specimen is sent to the reference laboratory for confirmation. If IgM antibody is detected, further IgM antibody tests are used to 'date', in terms of months, how recent a possible acute infection was, and is it likely, for example, to have occurred preconception.[14] When an 'at risk' pregnancy is identified, a specimen of amniotic fluid taken by amniocentesis can be examined for toxoplasma by PCR. This work is done by collaboration of the obstetrician and medical microbiologist/virologist or infectious diseases physician and the reference laboratory.

Toxoplasmosis is a primary disease of felids, with humans and other warm-blooded animals acting as the intermediate host. Kittens produce in excess of 10×10^6 oocysts/day. In order to become infectious, oocysts need to sporulate outside the cat, which takes place within 1–5 days, depending on the temperature and oxygen in soil or cat litter. Thus, cat litter carefully changed every day is unlikely to be a risk. Other sources of infection include raw pork and lamb, the handling of such animals, or hen eggs that may have been soiled in farms. General advice on limiting acquisition of toxoplasmosis is given below.

- Freezing food to –20°C is effective in killing oocysts, although domestic freezers may not achieve this temperature.
- Eggs should not be eaten raw.
- Do not consume unpasteurized milk (especially that from goats).
- Avoid touching eyes and mouth (mucous membranes) when handling raw meat.
- Meat should preferably cooked as 'well done'. Smoked or brine meat may still be infectious.
- Avoid ingestion of dried meats.
- Wash fresh fruit and vegetables thoroughly before consumption.
- Ensure hands are washed before and after cooking, or use gloves.
- Avoid direct contact with cat faeces, cat litter, and garden refuse.
- Disposable gloves are advised when these activities are necessary.
- Kitchen surfaces and utensils that have come into contact with raw meat should be washed and dried. Keep cats off these surfaces!
- Disinfect the cat litter box with near boiling water for 5 minutes after emptying the litter. If the litter box is cleaned every day, oocysts do not have the time to sporulate.
- Serological testing of cats is not warranted, as serology does not show whether the infected cat is excreting oocysts or not.

Mumps

The acute febrile illness associated with mumps is recognized to cause an excess of fetal loss in the first trimester. There is no convincing evidence that congenital defects or low birth weight is associated with mumps infection.[15]

The exanthems

The Coxsackie and ECHO viruses are associated with a range of rash-associated febrile illnesses. Infection during pregnancy is not associated with any particular risk to the fetus, although rarely they can result in abortion as a consequence of any febrile illness.[1, 16] Only hand-foot-and-mouth disease can be reliably diagnosed clinically. It is characterized by vesicular lesions on the hands, feet, and mouth, with the latter breaking down to form ulcers.[1] Pregnant women either in contact with a case of hand-foot-and-mouth disease, or who develop the characteristic lesions, can be told that there are no adverse consequences to the fetus, and can be reassured.[1]

It should be noted that congenital enterovirus infections can be acquired by the fetus in the last week of gestation, or more commonly perinatally, which occasionally rise to severe illness characterized by either myocarditis and/or hepatitis.

Hepatitis E virus

Hepatitis E virus (HEV) needs mention, because of the high rates of maternal mortality (up to 20%) associated with infection during pregnancy.[17] HEV is considered an imported infection from areas of the world such as the Indian subcontinent and Middle East. However, it is appropriate to test for HEV in any patient presenting with jaundice when all other likely causes have been excluded (see Chapter 9). Applicable to potential exposure to any infectious disease in pregnancy, it is prudent to recommend that travel to endemic areas of the world should be delayed until after the baby is born.

VACCINATIONS IN PREGNANCY

The clear benefit of vaccination before the child-bearing age is exemplified by the success of the rubella vaccine. In addition, passively acquired maternal antibodies to the tetanus toxin prevent neonatal tetanus. Live vaccines are not used, but it is considered safe to give certain killed vaccines, and the inactivated HBV, hepatitis A virus (HAV) and influenza vaccine can be given where there are clear indications, and the benefit outweighs the risk. The main reason for not giving killed vaccines is the potential for a suboptimal response due to the immunosuppressive effect of pregnancy.

SUMMARY AND KEY POINTS

In summary, the following points should be noted:

- The practice should establish guidelines for clinical and nursing staff to use so that there are set criteria, centred around the Quick Action Guides and the critical steps of 165.
- Regular training programs must emphasize the need for urgency, and prompt communication with the laboratory. Exposure to VZV in pregnancy is the classic example where the process not infrequently goes wrong!
- This underlines the importance of promptly contacting the medical microbiologist/virologist/infectious diseases physician when the pregnant patient has been exposed to any rash-like illness, or develops a rash.
- The pregnant patient who has been exposed to any rash-like illness, or develops a rash must be seen immediately and should not be kept waiting. The patient exposed to a rash-like illness such as chickenpox may be presenting late in the incubation period, and may now be infectious. For this reason when these patients are referred to the obstetric services (or another hospital), staff there must be informed in advance so that the patient is seen separately away from other ‘at risk’ individuals.

11

Antibiotic Guidelines

- Introduction
- Treatment guidelines for common infections

INTRODUCTION

This is an example of treatment guidelines that are appropriate for use in the community, and for use in adults (unless otherwise specified). Such guidelines should emphasize the risk that antibiotic use has in precipitating diarrhoea due to *Clostridium difficile* (CDAD). These guidelines are modelled on the document presented by the Health Protection Agency, *Management of Infection Guidance for Primary Care* (www.hpa.org.uk).[1] (Reproduced and adapted with permission of the UK Health Protection Agency.) For dosages in the UK see the *British National Formulary* (BNF), and the *BNF for Children*.[2, 3] National guidelines, along with manufacturers' recommendations should be used to draw up local guidelines. Included are recommendations that are appropriate in the USA; these are listed in italics. A single agent is used unless otherwise specified.

Some key points that should be included in local guidelines are:

- Most antibiotics have the capacity to precipitate CDAD. The risk however, varies between groups of antibiotics. The highest risk groups include the cephalosporins, fluorinated quinolones, and clindamycin.[1, 4–7] In general, these antibiotics should be avoided where a lower risk antibiotic is not contraindicated and is as effective in treatment of the condition. Other risk factors also need to be taken into account. *Clostridium difficile* is uncommon under the age of 20, it is also uncommon in young adults if they have not had contact with a health-care facility.
- Penicillin allergy. The precise nature of the allergy should always be questioned as from a patient perspective an adverse reaction such as diarrhoea may be seen as an allergy.
- For the penicillin-allergic patient where a cephalosporin can be used, and taking into account the risk of CDAD, an agent such as cefalexin can be appropriate. Based on local susceptibility patterns, the antibiotic will have activity against *Streptococcus pneumoniae*, groups A, C, G streptococci, and methicillin-sensitive *Staphylococcus aureus* (MSSA). It is thus useful to consider this option in the allergic patient, where the organism, e.g. group A streptococcus is resistant to erythromycin (and other macrolides) and tetracycline (doxycycline). See Chapter 5, **91**.
- In pregnancy, tetracyclines, quinolones, and high-dose metronidazole should be avoided. Short-term use of trimethoprim (unless low folate status or taking another folate antagonist such as an antiepileptic or proguanil) or nitrofurantoin (at term, theoretical risk of neonatal haemolysis) is unlikely to cause problems to the fetus.[1]
- Clarithromycin is cited here, as it has fewer side-effects than erythromycin, greater compliance as a q12h versus q6h for erythromycin, and generic tablets are similar cost.[1]
- Acute sore throat: Avoid antibiotics as 90% of cases will resolve within 7 days, and pain is only reduced by 16 hours.[1, 8] If Centor score 3 or 4 consider 3-day delayed or immediate antibiotics.[1, 9] (See Chapter 8, Quick Action Guide.)
- Acute otitis media: Avoid antibiotics as 60% are better in 24 hours without antibiotics, which only reduce pain at 2 days, and do not prevent deafness.[1, 10] Consider 3-day delayed or immediate antibiotics for children <2 years with bilateral acute otitis media (AOM), and all ages with otorrhoea.[1]
- Acute rhinosinusitis: Avoid antibiotics as 80% resolve in 14 days without antibiotics, and they only have a marginal benefit after 7 days.[1, 11, 12] Consider 7-day delayed or immediate antibiotic when there is fever >38°C, toothache, or high CRP.[1, 13]
- Acute cough or bronchitis: Antibiotics have little benefit if there are no co-morbidities. Symptom resolution can take up to 3 weeks.[14]
- It is essential that local, county, regional, state, or national surveillance data, and the recommendations from these are used. While local experience will influence use, it is recommended for example that trimethoprim should not be used for treating uncomplicated cystitis and pyelonephritis where resistance prevalence exceeds 20%. [15] The resistance rates of gonococci to quinolones in the USA means that these agents are no longer recommended for treating gonococcal infections.[16]

TREATMENT GUIDELINES FOR COMMON INFECTIONS

(Adult doses unless otherwise specified)

- Always review the previous microbiology results on the patient; for example has methicillin-resistant *Staphylococcus aureus* (MRSA), or has extended-spectrum β-lactamase (ESBL) 'coliform' been isolated in the recent past?
- Review all relevant cautions and contraindications in pregnancy, breastfeeding, renal and liver disease.

Suspected meningococcal disease

Administer antibiotic immediately and transfer urgently to hospital. Then inform local public health department.

If no history of penicillin allergy: Benzylpenicillin IV, or IM if a vein cannot be accessed:

Patient is 10 years and older	1200 mg
Patient is 1–9 years	600 mg
Patient is <1 year	300 mg

If penicillin cannot be given (e.g. due to allergy to penicillin), consider cefotaxime or ceftriaxone IV, or IM if a vein cannot be accessed:

Patient is 10 years and older	1.0 g
Patient <10 years check the BNF or manufacturer's recommendations.	

Community-acquired pneumonia (CAP) in the adult (see Chapter 8, Quick Action Guide)

Where urgent referral to hospital for CAP is delayed and/or life-threatening:

If no history of penicillin allergy: Benzylpenicillin IV, or IM if vein cannot be accessed: 1200 mg, or amoxicillin 1 g by mouth

If penicillin cannot be given (e.g. due to allergy to penicillin), consider cefotaxime or ceftriaxone IV, or IM if a vein cannot be accessed: 1.0 g

With azithromycin 500 mg or moxifloxacin 400 mg ONCE

Condition	No allergy to penicillins	Allergy to penicillins (or alternative regimes)
Respiratory tract infections		
Pharyngitis	Penicillin V 500 mg q6h for 10 days Penicillin V 1g q12h for 10 days Penicillin 1 g q6h for 10 days (if severe)	Clarithromycin 250–500 mg q12h for 5 days *Erythromycin 250–500 mg q12h for 7–10 days* Azithromycin 500 mg day 1, and the 250 mg q24h for 4 days.
Acute sinusitis	Amoxicillin 500 mg q8h for 7 days Penicillin V 250 mg q6h for 7 days	Doxycycline 200mg day 1, then 100 mg q24h for 6 days *Levofloxacin 750 mg q24h for 7–10 days* *Moxifloxacin 400 mg q24h for 7–10 days*
Second line	Co-amoxiclav 625 mg q8h for 7 days *Co-amoxicillin 825/125 mg q12h for 10 days*	
Acute otitis media (Give for 5 days)	Amoxicillin (See BNF for Children)	Erythromycin (See BNF for Children) *Levofloxacin 750 mg q24h for 5 days* *Moxifloxacin 400 mg q24h for 5 days*
Acute otitis externa	Clioqinol-flumetasone 2% acetic acid in 70% ethanol 2% acetic acid spray (Earcalm®)	2–3 drops morning and evening for 7–14 days (maximum) 2–3 drops morning and evening for 5–7 days As directed by manufacturer
It is important that the treatment in each ear is allowed to make contact with the lining of the canal by lying 'ear up' for 10–20 minutes for each ear.		
Acute cough/ bronchitis	Amoxicillin 500 mg q8h for 5 days	Doxycycline 200 mg day 1, then 100 mg q24h for 4 days
If pertussis is suspected, give erythromycin 500 mg q6h for 14 days, or azithromycin 500 mg day 1, and then 250 mg q24h for 4 more days.		
COPD – acute exacerbation	Amoxicillin 500 mg q8h for 5 days	Doxycycline 200 mg day 1, then 100 mg q24h for 4 days Clarithromycin 500 mg q12h for 5 days
	Co-amoxiclav 625 mg q8h for 7 days *Co-amoxicillin 825/125 mg q12h for 5–7 days*	*Levofloxacin 500 mg q24h for 5–7 days* *Moxifloxacin 400 mg q24h for 5–7 days*
The second-line option can be used when there is clinical failure with the first-line options.		

CAP Use CRB65 (Confusion, Respiratory rate >30/min, Blood pressure <90 systolic/60 or less diastolic, 65 years or older; score 1 for each) 0: Suitable for home treatment; 1 or 2: Consider hospital referral; 3 or 4: Immediate referral

Start antibiotics immediately

CRB65: 0

Amoxicillin 500mg q8h for 7 days

Clarithromycin 500 mg q12h for 7 days
Doxycycline 200 mg day 1, then 100 mg q24h for 6 days

CRB65: 1

Amoxicillin 500 mg q8h AND/OR (alone)

Clarithromycin 500 mg q12h for 7–10 days
Doxycycline 200 mg day 1, then 100 mg q24h for 6–9 days

Doxycycline 100mg q12h for 7–10 days
Azithromycin 500 mg q24h for 3 days OR 2 g STAT
Levofloxacin 750 mg q24h for 5 days
Moxifloxacin 400 mg q24h for 7 days

Conjunctivitis

Chloramphenicol 0.5% drops q2h, reducing to q4h, plus 1% ointment at night, OR Fusidic acid 1% gel q12h

Trimethoprim-polymyxin B sol 1gtt q3h for 7–10 days
Bacitracin-polymyxin B ophthalmic 1gtt q3–4 h for 7–10 days

Contact lens wearers and/or corneal ulceration, especially if pseudomonas suspected (discuss with ophthalmologist):

Ciprofloxacin 0.3% sol 1–2gtt q2h for 2 days then 1–2gtt q4h for 5 days
Levofloxacin 0.5% sol 1–2gtt q2h for 2 days then 1–2gtt q6h for 5 days
Ofloxacin 0.3% sol 1–2gtt q2–4h for 2 days then 1–2gtt q6h for 5 days

Continue treatment until at least 48 h after symptoms clear.
Most bacterial infections are unilateral, self-limiting, with a yellow-white mucopurulent discharge.

Urinary tract infections

UTI – cystitis*

Trimethoprim 200 mg q12h

Nitrofurantoin 100 mg m/r q12h

Prescribe antibiotics for 3 DAYS FOR WOMEN and 7 DAYS FOR MEN

If treatment failure occurs, patient should submit MSU for microbiological investigation.

UTI – pregnancy**

Trimethoprim 200 mg q12h for 7 DAYS (give folic acid if in first trimester) (off-label)

Nitrofurantoin 100 mg m/r q12h for 7 DAYS
Cefalexin 500 mg q12h for 7 days

UTI – pyelonephritis

Co-amoxiclav 625 mg q8h for 14 days
Co-amoxicillin 825/125 q12h for 10 days

Ciprofloxacin 500 mg q12h for 7 days

Trimethoprim can be used, if organism is susceptible; 200 mg q12h for 14 days

No response in 24 hours, refer to hospital.

UTI – recurrent post-coital***

Trimethoprim 100 mg STAT

Nitrofurantoin 50–100 mg STAT (off-label)

Either use STAT post-coital or once at night; advise complete bladder emptying after coitus.

UTI – children

Less than 3 months of age refer to paediatric specialist

Refer to **60**, **61**, Chapter 3

Lower UTI: treat for 3 days. Trimethoprim, nitrofurantoin, cefalexin or amoxicillin (if susceptible), as per BNF paediatric dosages, or refer to manufacturers' recommendations

Upper UTI: treat for 7–10 days. Co-amoxiclav, as per BNF paediatric dosages, or refer to manufacturers' recommendations

*ESBL 'coliforms' are often sensitive to nitrofurantoin, and fosfomycin (in the UK available on a named patient basis); check susceptibility profile, and contact the medical microbiologist for advice.

**Short-term use of nitrofurantoin is unlikely to affect the fetus. Avoid trimethoprim if low folate status or taking folate antagonist, e.g antiepileptic or proguanil.[1]

***Post-coital antibiotic is as effective as nightly prophylaxis; advise bladder emptying after coitus. This should be considered in sexually active women who have three or more UTI each year.

Skin, soft tissue, and dermophyte infections	**ALWAYS CONSIDER NEED FOR MRSA COVER**	
Impetigo	Flucloxacillin* 500 mg q6h for 7 days *Dicloxacillin 250 mg q6h for 10 days*	Clarithromycin 500 mg q12h for 7 days *Erythromycin 250 mg q6h for 10 days* *Clindamycin 300–400 mg q8h for 10 days*
	Topical antibiotics can be used for localized infections, <2 cm diameter. For general use, fusidic acid can be applied; mupirocin should be reserved for MRSA. Both are applied q8h for 5 days. (In eczema, using antibiotics, selects for resistant bacteria, and does not improve healing, unless there are visible signs of infection. For *infected* eczema, use treatment for impetigo).	
Cellulitis	Flucloxacillin* 500 mg q6h for 7 days *Dicloxacillin 250 mg q6h for 10 days*	Clarithromycin 500 mg q12h for 7 days Clindamycin 450 mg q6h for 7 days *Azithromycin 500 mg for 1 day, then 250 mg q24h for 4 days* *Clarithromycin 250 mg q12h for 7–10 days* *Clindamycin 300 mg q8h for 7–10 days*
	If the patient is febrile, consider admission for intravenous antibiotics.	
Leg ulcers	Flucloxacillin* 500 mg q6h for 7 days *Dicloxacillin 250 mg q6h for 10 days*	Clarithromycin 500 mg q12h for 7 days *Clindamycin 300 mg q8h for 7–10 days*
	Note that bacteria will always be present, and that antibiotics do not improve healing. The collection of swabs for culture and the use of antibiotics should only be considered if there is, for example, cellulitis, increased pain, ulcer enlargement, or pyrexia (see Chapter 5).	
MRSA	Doxycycline 200 mg q24h, PLUS rifampicin 600 mg q12h OR fusidic acid 500 mg q8h, for 7 days	
OR	Trimethoprim 200 mg q12h, PLUS rifampicin 600 mg BD OR fusidic acid 500 mg q8h, for 7 days	
	*Clindamycin 300 mg q8h for 7–10 days***	

*Flucloxacillin (and dicloxacillin) has good activity against group A streptococcus, and can be used for 'mild/moderate' infections as monotherapy when MRSA is not likely.
***Most CA-MRSA strains in the USA are likely to be sensitive to clindamycin (check local/national susceptibility trends).*

Bites – animal	Co-amoxiclav 625 mg q8h for 7 days *Co-amoxicillin 825/125 q12h for 7 days*	Metronidazole 400 mg q8h PLUS doxycycline 100 mg q12h for 7 days (Seek advice for children)
	• Surgical toilet is essential • The risk for tetanus and rabies must be assessed (see appendix Chapter 5).	
	Use these as treatment or prophylaxis. All bite wounds should be reviewed at 24 and 48 hours.	
	Prophylactic antibiotics are advised for puncture wounds, bites to the hand, foot, face, joint, tendon, and ligament. Irrespective of the site of the bite, antibiotic prophylaxis should be given to the immunocompromised, the diabetic, the elderly, and asplenic individuals.	
Bites – human	Co-amoxiclav 625 mg q8h for 7 days *Co-amoxicillin 825/125 q12h for 7 days*	Metronidazole 400 mg q8h PLUS clarithromycin 500 mg q12h for 7 days OR doxycycline 100 mg q12h for 7 days
	• The risk for HIV, HBV, and HCV must be assessed (see appendix Chapter 5).	
	Use these as treatment or prophylaxis. All bite wounds should be reviewed at 24 and 48 hours.	
	Antibiotics as prophylaxis are advised for puncture wounds, bites to the hand, foot, face, joint, tendon, and ligament. Irrespective of the site of the bite, antibiotic prophylaxis should be given to the immunocompromised, the diabetic, the elderly, and asplenic individuals. Surgical toilet is essential.	

Scabies	Permethrin	5% cream	2 applications, 1 week apart
	Malathion	0.5% aqueous liquid	2 applications, 1 week apart
	Treatment should be applied to the whole body, including scalp, face, neck, ears, and under the nails.		
	All household contacts should preferably be treated at the same time, or within 24 hours.		
	Ivermectin	*200 µg/kg STAT, then repeat 2 weeks later (contraindicated in pregnancy)*	

Dermatophyte proximal fingernail or toenail	Amorolfine 5% nail lacquer 1–2 times a week for 6 months for fingers, and 12 months for toes		
	Ciclopirox 8% nail lacquer, q12h for 48 weeks *Naftifine gel topically q12h for 48 weeks*		
	Terbinafine 250 mg q24h for 6–12 weeks for fingers, and 3–6 months for toes.		
	Itraconazole 200 mg q12h for 7 days each month 2 courses for fingers, and 3 courses for toes; after 7 days of treatment, skin/nail tissue levels of itraconazole are therapeutic for up to 3 weeks (Also active against yeasts and nondermatophtye moulds)		
	Nail clippings and under nail scrapings (primarily nail bed infection) and any friable tissue should be collected. Treatment should only be prescribed if there is microscopic and/or culture evidence of dermatophyte infection.		
Dermatophyte skin infection	Topical 1% terbinafine q12h for 1–2 weeks OR topical undecanoic acid or 1% azole 1–2 times daily for 4–6 weeks		
	If intractable consider oral itraconazole for 200 mg q12h for 7 days, *or terbinafine 250 mg q24h for 2–4 weeks*		
	'Ice Cool' skin sprays containing ether can give prompt relief from the distracting discomfort of 'athlete's foot'.		
	If the infection is not localized or does not respond to treatment, skin scrapings should be collected. Scalp infections should be discussed with a dermatologist; see tinea capitis, Chapter 6.		
VZV – chickenpox		Aciclovir	800 mg 5 times a day for 7 days
	OR	Valaciclovir	1 g q8h for 7 days
	OR	Famciclovir	250 mg q8h for 7 days
	If the patient is pregnant or immunocompromised, seek advice. In the immunocompetent child, the value of antivirals is minimal, but should be considered in ALL adults. Treatment is most effective when given within 24 hours of the appearance of the rash.		
VZV – herpes zoster	Treatment options as above		
	Always treat if ophthalmic zoster, Ramsey–Hunt syndrome/eczema; refer to the ophthalmologist.		
	For nonophthalmic zoster, treat patients over 50 years if within 72 hours of appearance of the rash.		
Gastrointestinal infections			
Gastroenteritis	Check travel, food and and risk assess for *Clostridium difficile*. Fluid replacement with oral rehydration salts is very important for children, or fluids such as 'flat' coca cola for adults). Antibiotics should not usually be given, especially if there is bloody diarrhoea (*Escherichia coli* O157). Send stool specimen.		
	If patient is systemically unwell, and campylobacter suspected (undercooked chicken and 'grippy' abdominal pain), consider clarithromycin 250–500 mg q12h for 5–7 days.		
Traveller's diarrhoea	Limit prescription (ciprofloxacin 750 mg single dose, or 500 mg q12h for 3 days) to those travelling to remote areas, or in whom an episode of infectious diarrhoea could be dangerous. To be taken when diarrhoea develops. With prolonged ciprofloxacin use there is the risk of CDAD.		
	In areas with high levels of resistance to ciprofloxacin (Asia), can advise prophylactic bismuth subsalicylate (Pepto Bismol) 2 tablets q6h for 2 days.		
	Azithromycin 500 mg for 3 days (takes account of high levels of resistance of enteric pathogens to ciprofloxacin in certain countries).		

CDAD	Unnecessary antibiotics and/or PPI should be stopped. For mild disease (Chapter 7), specific antibiotic therapy may not be needed providing other precipitating factors can be stopped and patient can be monitored closely. Metronidazole 400 mg q8h for 14 days (response to treatment can take 4–6 days). For first relapse/reinfection repeat metronidazole course, OR vancomycin 125 mg q6h for 14 days. Avoid antimotility agents. A stool specimen should be collected for toxin testing. 70% of individuals respond to metronidazole within 5 days, and 92% within 14 days.[1] If the patient is pyrexial (>38.5°C), WCC >15 × 10^9/L, raised creatinine, and/or symptoms and signs of colitis, urgent referral to hospital must be considered (Chapter 7).

Helicobacter

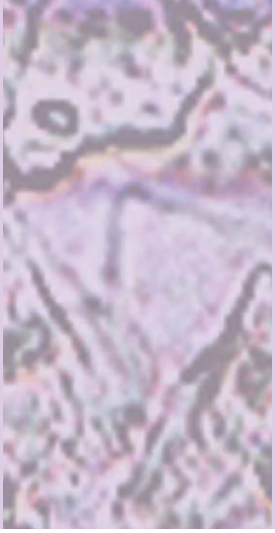
First line:		PPI (use the least costly)		q12h
	PLUS	Clarithromycin	250 mg	q12h when given with metronidazole
		OR	500 mg	q12h when given with amoxicillin
	PLUS	Metronidazole	400 mg	q12h
	OR	Amoxicillin	1g q12h	
			ALL FOR 7 DAYS	
Second line:		PPI (use the least costly)		q12h
	PLUS	Bismuthate	120 mg	q6h
	PLUS	TWO UNUSED ANTIBIOTICS:		
		Amoxicillin	1g	q12h
		Metronidazole	400 mg	q8h
		Tetracycline hydrochloride	500 mg	q6h
		RELAPSE OR MALTOMA GIVE 14 DAYS OF TREATMENT		

Threadworms	Mebendazole	100 mg once for patients 6 months or older (off-label <2 years)
	Piperazine/senna sachet	Use for children under 3–12 months of age 2.5 mL spoon once Repeat 2 weeks later
	Child <3 months, high standard hygiene for 6 weeks; see comment below)	
	Treat all household contacts, and ensure morning showering, and hand hygiene is advised. On day 1 wash all sleepwear, bed linen, towels, dust and vacuum.	
Entamoeba	Metronidazole 800 mg q8h for 5 days if only intestinal disease	
	Followed by cyst clearance with:	
		Diloxanide furoate 500 mg q8h for 10 days
	OR	*Iodoquinol 650 mg q8h for 20 days after meals*
	OR	*Paromomycin 25–35 mg/kg/day in 3 divided doses/day for 7 days with meals*
Giardia	Metronidazole 2 g q24h for 3 days OR metronidazole 400 mg q8h for 5 days	
	Metronidazole 250 mg q8h for 5–7 days	

Genital tract infections	Note that topical applications can weaken latex condoms and diaphragms; note the manufacturer's cautions. Advise women that protection from STI and pregnancy may be compromised. Abstain or use alternative contraception during, and for 5 days after treatment. It is best to use topical agents before sleeping, so that the supine form allows longer retention of the agent in the vagina.
Bacterial vaginosis	Metronidazole 400 mg q12h for 7 days, OR 2 g STAT OR metronidazole 0.75% vaginal gel 5 g applicator full for 5 nights OR clindamycin 2% cream 5 g applicator full for 7 nights
	Metronidazole 500 mg q12h for 7 days, OR 2 g once OR metronidazole 0.75% vaginal gel 5 g applicator full for 5 nights, OR clindamycin 2% cream 5 g applicator full for 7 nights
	Avoid the 2 g dose of metronidazole in pregnancy or breastfeeding. Topical treatment gives similar cure rates to systemic treatment, but is more expensive.

Candidiasis	Clotrimazole 500 mg pessary STAT at night Fluconazole, orally, 150 mg STAT *Butoconazole 2% cream 5 g intravaginally for 3 days** *Clotrimazole 1% cream 5 g intravaginally for 7–14 days** *Clotrimazole 2% cream 5 g intravaginally for 3 days** *(*Over-the-counter intravaginal agents)* *Fluconazole, orally, 150 mg STAT* *Terconazole 0.8% cream 5 g intravaginally for 3 days, or terconazole 0.4% cream 5 g intravaginally for 7 days* Topical and oral azoles have 80–95% cure.[1] Avoid oral antifungals during pregnancy.
Trichomoniasis	Metronidazole 400 mg q12h for 7 days OR metronidazole 2 g once *Metronidazole 500 mg q12h for 7 days OR metronidazole 2 g once* *Tinidazole 2 g ONCE* Avoid the 2 g dose of metronidazole or tinidazole in pregnancy or breastfeeding. Refer patient and partner to STD clinic.
Chlamydia	Doxycyline 100 mg q12h for 7 days OR azithromycin 1 g once 1 hour before or 2 hours after food (Erythromycin 500 mg q6h for 7 days, or amoxicillin 500 mg q8h for 7 days) (If erythromycin or amoxicillin are used, retesting should be done after 6 weeks, as these agents are less effective). Azithromycin (1 g STAT) can be used in pregnancy or breast feeding, but is off-label. *Doxycycline 100 mg q12h for 7 days, OR azithromycin 1 g once 1 hour before or 2 hours after food* *Erythromycin ethyl succinate 800 mg q6h for 7 days* *Levofloxacin 500 mg q24h for 7 days OR ofloxacin 300 mg 12h for 7 days*
Gonoccocus	Refer to local STD clinic guidelines.
PID	Metronidazole 400 mg q12h PLUS ofloxacin 400 mg q12h both for 14 days OR Cefixime 400mg ONCE, then metronidazole 400 mg q12h PLUS doxycycline 100 mg q12h both for 14 days It is essential to test for gonococcus as well as chlamydia, as the antibiotic resistance profile of gonococcus needs to be determined. *Ceftriaxone 500 mg IM ONCE, then doxycycline 100 mg q12h AND metronidazole 500 mg q12h both for 14 days*
Quinolones are no longer recommended in the USA for the treatment of gonorrhoea or related conditions such as PID.[16]	
Genital herpes	
First episode	Aciclovir 200 mg 5 times a day, or 400 mg q8h for 5 days. Use for longer if new lesions appear during treatment or healing is incomplete. Use 400 mg 5 times a day for 7–10 days in the immunocompromised, including HIV-positive patient. *Aciclovir 200 mg 5 times a day, or 400 mg q8h for 7–10 days* *Famciclovir 250 mg q8h for 7–10 days* *Valaciclovir 1 g q12h for 7–10 days*
Recurrent episode	Aciclovir 400 mg q8h for 5–10 days. *Aciclovir 400 mg q8h, or 800 mg q12h for 5 days, or 800 mg q8h for 2 days* *Famciclovir 125 mg q12h for 5 days, or 500 mg ONCE then 250 mg q12h for 2 days, or 1g q12h for 1 day* *Valaciclovir 500 mg q12h for 3 days or 1 g q24h for 5 days*
Suppression therapy	Aciclovir 200 mg q6h, or 400 mg q12h, possibly reduced to 200 mg q12h or q8h, increased to 400 mg q8h if recurrences recur on this treatment. Interrupt therapy at 6–12 months, reassess frequency and consider restarting therapy if two or more recurrences. *Aciclovir 400 mg q12h* *Famciclovir 250 mg q12h* *Valaciclovir 500 mg or 1g q24h*
Acute prostatitis	Ofloxacin 200 mg q12h OR ciprofloxacin 500 mg q12h OR trimethoprim 200 mg q12h, all for 28 days

Self-Assessment Review Cases



CHAPTER 1: Questions 1–5

Here are 20 scenarios that raise issues that can result in the primary care physician or nurse contacting the medical microbiologist/infectious diseases physician. You are invited to work through these, and compare your answers with those supplied as a self-assessment exercise.

1. A 19-year-old female student presents with a vaginal discharge. A HVS is taken which is reported as a profuse growth of group B streptococcus sensitive to penicillin and erythromycin. What would you do?

2. A 34-year-old woman presents with a vaginal discharge. A HVS is taken which is reported as growing a moderate growth of group A streptococcus, sensitive to penicillin and erythromycin. What would you do?

3. You receive the following report on a leg ulcer swab taken from an 86-year-old man. The report reads profuse growth of *Pseudomonas aeruginosa* sensitive to ciprofloxacin. The clinical details are 'long-standing leg ulcer'. What would you do?
(Two weeks later the patient returns to the practice/clinic, and there is an area of painful cellulitis adjacent to the ulcer. What would you do?).

4. You receive an HVS report on a 26-year-old woman with a vaginal discharge who is 20 weeks pregnant. The report states the presence of a heavy growth of group B streptococci and a heavy growth of candida. What would you do?

5. Your partner is away, and you see one of his patients, a 32-year-old woman who has ongoing diarrhoea, following a visit to the Middle East. She was initially given a 7-day course of ciprofloxacin for 'traveller's diarrhoea', when *Salmonella* Typhimurium was isolated from a stool sample. Her condition improved, then relapsed, and she is still unable to return to work. What would you do?

CHAPTER 1: Answers 1–5

1. • Group B streptococcus is a member of the normal vaginal flora, and is not recognized as a cause of a vaginal discharge. Therefore treatment is not indicated.
   • Group B streptococcus can be associated with wound or soft tissue infection after obstetric or gynaecological surgery; see Question 4.
   • Ensure other appropriate swabs have been taken at the first visit. If a sexually transmitted infection is likely, has referral to a STD clinic been done?

2. • Group A streptococcus can cause infections of the genital tract which may range from mild to severe. The patient must be treated with amoxicillin or erythromycin.
   • Infections of the genital tract can be caused by 'upper respiratory tract pathogens' including group A streptococcus, *Streptococcus pneumoniae*, and *Haemophilus influenzae*. Such infections also occur in pre-pubertal girls.
   • When these bacteria are identified in an HVS, treatment should always be considered. For group A streptococcus here, use the streptococcus 'A for always treat' guide.

3. • Clinically assess if there is evidence of infection, differentiating this from colonization/critical colonization. The reason for collecting the swab in the first place should be questioned; if there was no evidence of infection when the patient was first seen, a swab should not have been taken. Treatment is not warranted in this case. Ulcers can be overgrown by pseudomonas, and even if infection was present, a superficial swab may not sample the underlying pathogen; pseudomonas is low down on the list of likely pathogens. Treatment should be targeted at staphylococci and streptococci in the first instance (see Chapter 5).
   • Without full review of the patient, prescription of ciprofloxacin here would not only be unnecessary, but would put the patient at risk of CDAD.
   Two weeks later, the patient returns to the practice/clinic, and there is now an area of painful cellulitis adjacent to the ulcer.
   • There is now evidence of infection, and a swab, taken as close as possible to viable tissue, should be collected. As the most common bacteria are *Staphylococcus aureus* or group A, C, and G streptococci, flucloxacillin/dicloxacillin, or a macrolide for the penicillin-allergic patient, must be given (provided there is no risk of MRSA).

4. • Treat the candida with an antifungal pessary/cream.
   • Group B streptococcus is not a cause of a vaginal discharge.
   • Group B streptococcus can cause invasive disease in the newborn, especially in 'at risk' situations such as pre-labour rupture of membranes, and fever in the mother during labour. Specific protocols are in place in obstetric units to manage these situations. Antibiotic therapy during pregnancy does not eradicate carriage, and should not be given for this purpose.
   • Carriage of group B streptococci in pregnancy should be clearly recorded as an 'alert' in the patient's notes in the event of obstetric complications around the time of delivery, when treatment may be needed. Remember streptococcus 'B for birth'.
   • Group B streptococcus can be associated with wound or soft tissue infection after obstetric or gynaecological surgery.

5. • The condition of the patient should be assessed and advice given about fluid intake.
   • The patient should submit a further stool to determine if the salmonella is still present, and to see if there are other pathogens. Mixed infections when returning from abroad are not uncommom. OCP examination should be included on the request form. If *Entamoeba histolytica* is a possibility, then a 'hot stool' specimen is required as trophozoites will autolyze quickly (see Chapter 7).
   • Ensure that stool is examined for the toxin of *Clostridium difficile*. This infection is not restricted to the elderly, but also occurs in younger adults, and needs to be tested for in all adults who have, or develop, diarrhoea following consumption of antibiotics.
   • This episode may have unmasked another medical condition, and if the diarrhoea persists, further investigations should be considered. Inflammatory bowel disease and HIV infection can be considered.

CHAPTER 1: Questions 6–10

6. A laboratory report with the clinical details 'CSU long-term indwelling catheter, cloudy urine, + leukocytes and ++ nitrites on dipstick' states:

> Microscopy: WBC >100 × 10^6/L,
> RBC 20 × 10^6/L, no epithelial cells seen.
> Culture: Pure growth of *Pseudomonas aeruginosa* (>10^8 colonies/L) sensitive to ciprofloxacin.
> What would you do?

7. You review the following urine result:

> Microscopy: WBC 50 × 10^6/L,
> RBC 5 × 10^6/L, no epithelial cells seen.
> Culture: Pure growth of enterococcus (>10^8 colonies/L), sensitive to amoxicillin and nitrofurantoin.

   i. The same result was obtained from a routine urine screen of a 23-year-old primigravida who is 18 weeks pregnant. What would you do?
   ii. The same result was obtained from a 68-year-old female following a routine dipstick of the urine that showed a trace of protein. What would you do?

8. It is 4 o'clock on a Friday afternoon, and your next patient, who is 16 weeks pregnant, tells you that she was in contact with a child who has developed a chickenpox rash. What would you do?

9. A mother tells you that her child picked up a needle in the local park 2 hours ago, and is sure that the child pricked herself. What would you do?

10. A mycology result of nail clippings collected from a 50-year-old man with dystrophic toenails states:
    Microscopy: fungal elements seen.
    Culture no growth.
    What would you do?

CHAPTER 1: Answers 6–10

6. • The CSU should not have been taken as the patient is asymptomatic.
   • Bacteriuria is an inevitable consequence of catheterization longer than 4–5 days. There is nothing that can be done about this, and treatment should only be given if the patient is systemically unwell, for example with fever, rigors, confusion or increased confusion, loss of diabetic control. Antibiotics are not indicated in this case.
   • Antibiotics will select out more resistant bacteria or yeasts, and put the patient at risk of CDAD.

7. **i.** • If a carefully collected repeat MSU specimen shows no growth, the patient can be reassured.
   • A carefully collected repeat specimen grows the same organism; the patient is treated with a course of amoxicillin (or nitrofurantoin) for 7 days. This is because asymptomatic bacteriuria in pregnancy is associated with a significant risk of complications.
   • Follow-up urine specimens can be taken 7 and 14 days after completion of therapy. If either of these is positive, then consideration for antibiotic prophylaxis throughout the remainder of pregnancy would be discussed with the obstetrician. Local protocols should be used.

   ii. • Question why the urine was collected in the first instance; a trace of protein is not an indication for sending a specimen for MC&S.
   • Asymptomatic bacteriuria is not uncommon in this age group, and should be regarded as a 'normal' consequence of the ageing process.
   • There is no evidence to support the treatment of asymptomatic bacteriuria in the older/elderly patient, and treatment unnecessarily 'medicalizes' the condition, and puts the patient at risk of CDAD.

8. • Check the patient's chickenpox history. If she gives a definite history of chickenpox in the past, she is immune and can be reassured. This information should be documented in the patient's notes.
   • If there is no history of chickenpox, collect blood, and arrange for urgent VZV antibody testing by contacting the medical microbiologist now. Ensure that arrangements are in place so that if necessary the patient can be contacted with results either that night or the following day in situations where the result will not wait until after the weekend. Note that an individual with chickenpox is considered infectious from 48 hours *before* the rash appears, and the minimum time from infection to the rash appearing is 10 days. The essential detail is to find out when the exposure took place, and record this on the request form.
   • If testing shows that VZV antibodies are detected, the patient can be reassured.
   • If testing shows that VZV antibodies are not detected, VZIG has to be given. VZIG must be given within 10 days of the exposure.

9. • Inform the mother about the risks of contracting the blood-borne viruses (HBV, HCV, HIV). The amount of fluid inside the needle will be minimal, will likely have dried, HIV and HCV are unlikely to survive, and the overall risk is thus minimal.
   • Take baseline blood for long-term storage. Laboratories will store frozen serum from 'sharps' injuries for up to 2 years.
   • A rapid course of HBV vaccine should be started. Following the first injection, further doses are given at 1 and 2 months.
   • Consider further counselling and follow-up testing. This could either be with the paediatrician or infectious diseases clinic.

10. • The presence of fungal elements on microscopy confirms the diagnosis.
    • In up to 50% of cases where fungal elements are seen on microscopy, a dermatophyte is not cultured.
    • The patient should be treated with an appropriate antifungal agent, e.g. terbinafine.

CHAPTER 1: Questions 11–20

11. A 23-year-old medical student returned from an elective period in Malawi 6 months ago. He is concerned because one of his friends who accompanied him has had schistosomiasis diagnosed on a urine specimen. They both swam frequently in Lake Malawi. A MSU submitted for ova, cysts, and parasites is reported as negative. What would you do?

12. A young adult male comes to see you with a 3-day history of vomiting and diarrhoea. He attended a wedding reception at a local hotel 4 days previously and states that a number of other guests have been unwell with similar symptoms. What do you do?

13. A HCW in your practice/clinic has had the full course of vaccination for HBV. A subsequent test for HBV surface antibody is negative. The same result is obtained after a booster injection. What would you do?

14. A laboratory report on a specimen from a patient with a family history of HBV states:
HBsAb positive/HBcAb positive/HBsAg negative.
What does this mean, what would you do, and what would you tell the patient?

15. A laboratory report on a specimen from a patient with a family history of HBV states:
HBsAg positive/HBcAb positive.
What does this mean, what would you do, and what would you tell the patient?

16. A laboratory report on a patient with a history of IDU states:
HCV antibody positive.
What does this mean, what would you do, and what would you tell the patient?

17. A laboratory report of a stool specimen with the clinical details 'Recent campylobacter; ? clear' states: campylobacter still present. What would you do?

18. You receive the following report on a leg ulcer swab taken from an 86-year-old man. The report reads 'Profuse growth of group A streptococcus sensitive to penicillin and erythromycin'. The clinical details are 'Long-standing leg ulcer, now surrounded with painful and red cellulitis'. What do you do?

19. The laboratory report on a swab taken from a 29-year-old sportsman with otitis externa states: Profuse growth of *Pseudomonas aeruginosa*. What would you do?

20. The nurse manager at the nursing home you oversee telephones to say that three elderly patients have developed diarrhoea overnight. What would you do?

CHAPTER 1: Answers 11–20

11. • Correct specimen collection is important, as failure to do so, as in this case, can give a false negative result. Ideally, a terminal urine specimen should be collected after light exercise between the hours of 12 midday and 3 o'clock in the afternoon. The last 5–10 mL associated with the contraction of the trigone should be collected into a sterile, white-topped, preservative-free, container.
    • Serology for schistosoma antibodies (clotted blood sample) should be done, but can be negative if taken too early after exposure. Blood should not be collected until 12 weeks after the last exposure. A positive result warrants treatment with praziquantel.

12. • Assess the patient's clinical condition, advise the patient how to collect and submit a stool for culture, and advise supportive treatment.
    • The patient should be advised of the likely infectious nature of the gastroenteritis, the importance of hand washing and to avoid food preparation. All patients with gastroenteritis should be regarded as potentially infectious, and should be excluded from normal activities until at least 48 hours after being free of diarrhoea and/or vomiting (see Chapter 7). The patient should inform his occupational health department.
    • Public health should be informed immediately of a possible food-borne outbreak.

13. • It is important to check that the vaccine has been given at the correct intervals, and the tests for antibody were done at the appropriate time.
    • Has vaccine been delivered into the deltoid muscle? In overweight patients, a short needle may only penetrate fat, where the immune stimulus is negligible.
    • A repeat course of vaccination is completed, with a longer needle used, as necessary, to reach the muscle; HBsAb levels are tested 6 weeks later.
    • If HBsAb is not detected, the HCW should be counselled to have their HBcAb and HBsAg status determined.
    • If these are negative, the individual is not a chronic carrier, but is a nonresponder to the HBV vaccine. They should be advised about the risk of infection associated with EPPs, according to local OHD protocols.
    • If the HCW is identified as a carrier of HBV (HBcAb and HBsAg positive), they must be managed by the individual's OHD. Public health should be informed. Refer the HCW to a hepatologist for management of the condition.

14. • HBcAb, while not being protective, show that the patient has been infected with HBV in the past.
    • The presence of HBsAb, which confer protection, shows that the patient has developed natural immunity following the acute infection, which may have been an asymptomatic infection many years ago.
    • The patient can be reassured that he/she is naturally immune to HBV, and poses no risk to others. Public health should be informed, in order to screen other family members.

15. • The presence of HBsAg, shows that the patient is infectious, and is likely to be a carrier of HBV. (Note, however, that acute infection has to be excluded; see Chapter 9).
    • The patient needs to be counselled about this, and the risk to others. Public health should be notified. Further management of the patient can be discussed with the medical microbiologist/infectious diseases physician, with a view to referral to the hepatologist.
    • Where appropriate, occupational health should be involved.

16. • This result only shows that the patient has been infected with HCV in the past. HCV antibodies do not confer immunity. A positive antibody result on its own is insufficient information to manage the patient.
    • The presence of HCV RNA by PCR must be determined. Individuals who are RNA positive are chronically infected. Risks should be explained to the patient, e.g. alcohol use and the risk of hepatocellular carcinoma. Public health should be informed and the patient referred to the hepatologist.
    • The individual who is HCV antibody positive, but is RNA negative *on two consecutive samples* is not chronically infected. The patient 'cleared' the virus after the acute infection. Note that there are at least six genotypes, and that heterogenous antibodies are produced during infection, which *do not* confer immunity to HCV infection.

17. • Providing the patient is better, there is no need to send a further specimen. The condition is managed clinically with the vast majority of infections improving without intervention apart from fluid replacement. One is not looking for microbiological clearance with this organism either from a clinical or public health perspective. For a minority of patients, symptoms persist and in this setting antibiotics, usually a macrolide, together with fluid replacement would be indicated.
    • Person-to-person transmission of campylobacter is very uncommon.
    • Demonstration of clearance is required for certain pathogens using defined protocols for *Salmonella typhi/paratyphi*, *Escherichia coli* O157, and *Shigella dysenteriae* (see Chapter 7).

18. • This group A streptococcus infection clearly warrants treatment.
    • The patient should be reviewed and the condition of the ulcer assessed. The notes state that the patient was started on oral flucloxacillin after the swab was taken 2 days ago.
    • If the infection has improved, the treatment with flucloxacillin should be completed. Note that flucloxacillin has good activity against group A streptococcus, in addition to methicillin-sensitive *Staphylococcus aureus* (see Chapter 2).
    • If the infection has not improved, or has deteriorated, the medical microbiologist should be contacted, or immediate referral to the hospital considered.

19. • *Pseudomonas aeruginsosa* is found in domestic and recreational water supplies, and can be associated with 'swimmer's ear'. Prevention of the condition relies on good aural toilet, with ears being carefully dried after exposure to water.
    • One effective treatment is a topical solution of 2% acetic acid in 70% alcohol. This creates an acidic environment which kills pseudomonas (see Chapter 8).
    • Note that in older diabetic patients, and immunocompromised patients, *Pseudomonas aeruginsosa* can cause 'malignant otitis externa', with severe ear pain and facial nerve palsy. There should be immediate referral to the ENT surgeon.

20. • It is very important to assess the situation in person by visiting the home, and determine if there are other causes of diarrhoea (e.g. aperients), and assess the clinical condition of the affected individuals. The community infection control nurse should be present as well.
    • The likely causes should be considered, and antibiotic prescription should be reviewed; CDAD and norovirus are the most likely causes if this is infective in nature, but outbreaks with other organisms do occur.
    • A stool specimen must be collected from all affected individuals where possible, requesting MC&S, and CDT testing and norovirus.
    • Assessment of the affected patients must be done, and referral to hospital considered. If patients are sent into hospital then ambulance control and the hospital need to be informed in advance so that they can take precautions to minimize any risk of spread.
    • Public health officials should be informed. An 'outbreak' meeting should be held promptly with the nursing home manager, primary care physician, senior carer, community infection control nurse and public health representative in attendance. The medical microbiologist should be informed.

Appendix

Additional information about specific organisms and conditions is given in this Appendix for chapters 4, 5, 6, 7 and 9.

CHAPTER 4

Actinomyces	
Organisms	*Actinomyces israelii* Actinomyces-like organisms (ALO) are usually reported when they are seen in Pap smears. Actinomyces are minor members of the normal vaginal flora, but may come to prominence in the setting of intrauterine contraceptive device (IUCD) use. These organisms can be detected within several years of IUCD use, with a significant increase in prevalence after 4 years; the IUCD provides a surface that supports growth. Actinomyces rarely cause invasive disease in the uterus.
Specimen collection	When an IUCD is removed, and sent to the laboratory it is used to inoculate selective agar. Plates are incubated for 10 days; actinomyces are slow-growing anaerobes, and can be difficult to culture.
Treatment	When ALO are detected in the Pap smear of a woman with an IUCD *in situ*, conservative treatment is recommended, and the IUCD can be left *in situ*.[18,19] When the IUCD has been removed in these circumstances, the cervical cytology usually returns to normal within 1–2 menstrual cycles.[19] If there is pain, cervical discharge, or bleeding, the IUCD should be removed, and the situation monitored. If symptoms are still ongoing, or there are systemic symptoms such as fever, antibiotics are required, and the patient should be referred to the gynaecology department. Amoxicillin plus doxycycline or metronidazole for 2–3 weeks is advised.[18] More aggressive management is required for patients with pelvic abscesses, although a trial of antibiotics is recommended for smaller abscesses (up to 8 cm in diameter.[18] Note that actinomyces are resistant to metronidazole; this agent is given for general anaerobic cover).
Complications	These include actinomyces ovarian, pelvic and omental abscesses, which are uncommon.

Bacterial vaginosis (BV)

Organisms	*Gardnerella vaginalis* is the organism characteristically associated with BV, and in addition the anaerobes *Prevotella* spp. and *Mobiluncus* spp. are also associated with the infection. The cause of BV is unknown, but it is likely that usual minor members of the vaginal flora are able to overwhelm the protective lactobacilli, and the normal acid milieu that they create. The pH of the vagina rises from below 4.5 to a pH of 7.0, with complete disruption of the normal flora of the vagina.
Specimen collection	In the setting of a thin, white-grey homogeneous discharge, with increased (fishy) odour, an HVS should be collected. The pH of the discharge should be checked with a pH strip, and addition of 10% KOH to a film on a glass slide will release a strong 'fishy' odour. 'Clue cells', epithelial cells with numerous gardnerella attached to them seen in either 'wet preps' or gram-stained specimens (with absence of the normal vaginal flora) confirms the diagnosis. Culture of gardnerella should not be performed as it is too sensitive, and a positive culture does not correlate with clinical symptoms. If there is any risk of STI, a screen for chlamydia and gonococcus should be done.
Treatment	Treatment is with either oral or intravaginal metronidazole, or intravaginal clindamycin.
Complications	BV should be actively diagnosed and treated. The condition is associated with a higher incidence of endometritis after abortion, vaginal or Caesarean delivery, PID, pre-term delivery, spontaneous abortion. It can be a cause of marital disharmony.

Balanitis

Organisms	*Candida albicans* and non-*albicans* spp. Other organisms include gardnerella, anaerobes gonococcus and chlamydia (associated with urethritis), HSV and syphilis (associated with ulceration), and trichomonas. Group A streptococcus can arise as a result of fellatio; there may be associated trauma. Young boys can also have balanitis. When group A streptococcus is found in the urine of a young boy, the foreskin (if present) should be examined. Group A streptococcus is unlikely to cause a UTI. Anaerobes may also be identified in a swab. Candida balanitis can be diagnosed by a white cheese-like film on the glans and foreskin, which is easily rubbed off to reveal an erythematous base. The partner may have current vaginal candidiasis. Balanitis associated with a fish-like odour can occur when a partner has bacterial vaginosis. Chemical balanitis can be associated with soaps, condoms, lubricants, and feminine hygiene sprays. It is prudent to check a blood glucose in the male patient with severe or recurrent candida balanitis. An HIV test should also be considered.
Specimen collection	Appropriate swabs should be collected to confirm the diagnosis. In a sexually active male with urethritis, a FCU for chlamydial and gonococcal NAAT should be collected.
Treatment	The patient should be advised to avoid contact with irritants, e.g. soap. The glans and foreskin should be carefully bathed twice a day with a weak saline solution (this can be made by adding a level teaspoon of salt/100 mL of boiled water, which is allowed to cool before use). Candida infection is treated with a topical imidazole, which should be continued for 2–3 days after symptoms resolve; the usual course is 7 days. Oral fluconazole is often preferred by the patient; a single dose of 150 mg is recommended. Balanitis associated with gardnerella infection should be treated with metronidazole for 7 days. Balanitis following fellatio should be treated with 7 days of amoxicillin or clarithromycin.
Complications	The rare complication of necrotizing fasciitis of the penis can occur with a group A streptococcal infection; urgent surgical referral is required.

CHAPTER 4 – *continued*

Candidiasis

Organisms	*Candida albicans* and *non-albicans* spp.
	The majority of cases are caused by *Candida albicans.* In the setting of recurrent infection, the medical microbiologist should be contacted to discuss full identification of the candida, and the need for susceptibility testing.
	The vaginal pH is usually <4.5.
Specimen collection	In the setting of pruritis, dysuria, burning on micturition, vaginal erythema, and a thick curdy discharge, the diagnosis can be made clinically (see Quick Action Guide). A 'wet prep' of an HVS that shows typical candida hyphae is usually diagnostic. The yeast is cultured on selective fungal media. It is important to note that as culture is a sensitive test, scanty numbers of candida reported on culture usually represent normal vaginal flora.
	Mixed infections with BV and trichomonas can occur.
Treatment	Treatment is available with a range of intravaginal agents or oral fluconazole (see Chapter 11).
	Loose fitting cotton underwear should be worn and changed regularly.
	Patients with recurrent candidiasis, and no underlying condition should be discussed with the medical microbiologist/infectious diseases or STD physician. A specimen should be collected and full identification and antifungal susceptibility testing done. Occasionally, organisms such as *Candida glabrata* are identified, which may require more directed and specific treatment. The sexually active patient with recurrent candidiasis should be offered an HIV test.

Chlamydia

Organisms	*Chlamydia trachomatis*
	Chlamydia are intracellular organisms, and when a swab is taken, any pus must be removed first so that cells are collected. This applies to both genital and conjunctival specimens.
	Asymptomatic infection is common, and it is for this reason that voluntary screening should be available. Symptoms are often nonspecific, occasionally with urethritis.
Specimen collection	It is important to take the correct specimen from the symptomatic patient (**72–85**); ECS should be collected with speculum examination. Discharge should be removed from the cervical os, and an ECS collected for NAAT. For males a FCU, and a urethral swab can be collected for chlamydial and gonococcal PCR; see **78–85**.
	Testing should not be within 5 days of the last sexual contact, as this is within the incubation period of the organism.
	Sexual contacts, including those in the last 6 months should be traced, as a significant percentage will also be positive. Tests for other STD need to be done.
	For community screening programs, a self-taken vulvovaginal swabs (women), or a FCU (men) can be sent for chlamydia NAAT.
Treatment	Treatment for uncomplicated infection is with a single dose of azithromycin, or doxycycline for 7 days (see Chapter 11).
	Pregnant patients can be treated with amoxicillin or erythromycin, but a test of cure is required at 5–6 weeks.
Complications	Acute and chronic PID, infertility, conjunctivitis, neonatal infection, Reiter's syndrome, and Fitz–Hugh–Curtis syndrome.

Genital herpes

Organisms	Herpes simplex virus 2 and 1 (HSV2 and HSV1) HSV2 is essentially exclusive to the genitals, whereas HSV1 is primarily associated with oral herpes, but is increasingly seen with genital herpes. HSV2 infections are generally more severe, with increased recurrence rate. Transmission is highest when an individual is symptomatic, but most transmissions occur from an asymptomatic individual who may have been infected months or years previously. Transmission is by direct contact, and includes nonpenetrative, e.g. oral–genital sex. Infections are classified as primary, the first symptomatic episode in a previously uninfected individual, or nonprimary first episode in a person infected, e.g. with HSV2, who is then infected with HSV1. Recurrent infection occurs when there is symptomatic secondary disease with either HSV1 or HSV2.
Specimen collection	Vesicles should be gently opened, and a swab 'rolled' in the base of the ulcer, and then shaken in VTM. While culture was the previous 'gold standard', PCR for HSV1 and HSV2 is now routine.
Treatment	A first episode should be treated for 5 days or longer, with oral aciclovir, famciclovir, or valaciclovir. Treatment should be started on the clinical diagnosis, and not be delayed until results are available. Recurrent infections should be treated with intermittent or suppressive therapy, and is advised for a person with six or more episodes a year; the patient needs referral to the STD clinic. Topical agents are not recommended.
Complications	Genital herpes in the perinatal period can have devastating consequences for the newborn. The pregnant patient with primary or recurrent infections must be managed by the obstetrician and virologist. Aseptic meningitis is a recognized complication of HSV2 genital infection. It is usually a mild self-limiting condition that can be recurrent in nature.

Neisseria gonorrhoeae

Organisms	Gonococcus is a gram-negative diplococcus that is oxidase positive, and metabolizes glucose, but not lactose, maltose, or sucrose. It is a labile organism, does not grow on simple nutrient agar, and does not tolerate drying. It grows optimally at 35–37°C in an atmosphere of 5% CO_2. As it is found in sites where there are high concentrations of saprophytic bacteria (cervix, pharynx, rectum), selective media containing antibiotics, usually a modified 'chocolate' agar is used for isolation. Antibiotic resistance is a major problem. The appearance of strains that produce plasmid-mediated ß-lactamase, as well as those with chromosomally-mediated reduced affinity to penicillins has made the use of penicillin and amoxicillin redundant in many parts of the world. Quinolones and the tetracyclines are important agents, but resistance to these agents is not uncommon, with mechanisms such as mutations to the DNA gyrase (quinolones) and efflux from the cell (tetracyclines) being important. The infection is usually symptomatic in males with urethritis, but can be asymptomatic in females with uncomplicated infection, or they may only have minor symptoms, for which medical intervention is not sought.
Specimen collection	As this is a labile organism, reliable culture is dependent on the appropriate facilities, such as those in STD clinics, and patients should preferably be referred. If this is not possible, a FCU, swabs for culture and PCR can be collected. A slide can also be prepared for gram stain. Where there are facilities in primary care, culture plates can be inoculated immediately stored in 'sandwich boxes' with a CO_2 environment, and transported to the laboratory within 5 hours.[12] There are a number of NAAT tests available, often as dual tests for chlamydia and gonococcus. These tests are not significantly more sensitive than 'gold standard' culture. However, as they have high specificities for gonococcus (>99%), they are more practical than culture in the community setting, and can be used in FCU (males), ECS and urethral swabs. As the organism is associated with pharyngitis and proctitis, specimens should be collected from these sites. This should be the domain of STD clinics.
Treatment	The antibiotic susceptibility profile of gonococcus varies considerably, and empirical treatment for uncomplicated infection (urethritis in males; cervicitis/urethritis in females) should be based on local, regional, and national data. In areas where penicillin resistance is uncommon, amoxicillin and probenicid as a single dose can be given. Other single dose regimens include azithromycin 2 g, and ceftriaxone 500 mg (given IM). The use of quinolones and tetracyclines should be determined by local and regional susceptibility data.
Complications	Complications include PID, disseminated gonococcus, including septic arthritis and tenosynovitis, and prostatic abscess formation.

CHAPTER 4 – *continued*

Pelvic inflammatory disease (PID)

Organisms	PID is mainly associated with *Chlamydia trachomatis* infection. *Neisseria gonorrhoeae* should always be considered in diagnosis, and treatment. *Gardnerella vaginalis*, *Mycoplasms hominis*, anaerobes, and 'coliforms' are associated with chronic PID. Chlamydia and gonococcus, followed by other organisms, ascend the uterus to set up infection in the fallopian tubes, and uterine adnexae. Inflammation and fibrosis, in the fallopian tubes in particular, give rise to the symptoms and signs of pelvic pain and cervical excitation tenderness. The clinical diagnosis is more likely to be correct in sexually active women where the prevalence of STD is higher. Referral for laparoscopic confirmation can be done as necessary.
Specimen collection	Referral to the STD clinic is the best option. If this is not possible, ECS for chlamydia (NAAT) and gonococcus culture should be done. Culture of gonococcus is best, in order that susceptibility profile can be determined. If NAAT is done, positive PCR should be followed up for repeat testing, using culture. Pregnancy testing and analysis of urine for UTI should be considered.
Treatment	Following the clinical diagnosis, and collection of swabs, treatment must be started. Patients should be followed up 72 hours later to ensure that there is improvement. Analgesia should be given as needed. Treatment options are given in Chapter 11, which for the USA, take into account the fact that quinolones are no longer recommended for the treatment of gonorrhoea and related conditions such as PID.
Complications	Chronic PID, ectopic pregnancy, tubo-ovarian abscess.

Trichomoniasis

Organisms	*Trichomonas vaginalis* Trichomoniasis is a sexually transmitted disease, and is the most common STI in the USA. Risk factors include a change in sexual partner, sex more than twice a week, and other co-existent STI. The finding of trichomonas in a patient should be seen as a marker of other STI, which should be actively sought. The vaginal pH is >4.5.
Specimen collection	In the setting of pruritis, dysuria, and a yellow frothy discharge with increased odour, an HVS should be collected and sent to the laboratory for examination. If the laboratory does 'wet preps', the examination should be within 6 hours of collection; refrigeration can prolong the viability of the organism. It is preferable that laboratories do acridine orange staining, as nonviable protozoa can be seen. Some laboratories use culture methods to identify trichomonas. The organism may be reported by the laboratory as an incidental finding in urine. Because of the risk of associated STD, a full screen for chlamydia and gonococcus should be done, and the patient referred to the STD clinic.
Treatment	Treatment is with metronidazole or tinidazole (see Chapter 11).
Complications	The condition is associated with a higher incidence of endometritis after abortion, vaginal or Caesarean delivery, PID, pre-term delivery, and spontaneous abortion.

Urethral syndrome in women

Urethral syndrome is a condition where there is dysuria, frequency, urgency, and nocturia in the absence of a significant bacteriuria, defined as $>1.0 \times 10^8$ bacteria/L. Kunin *et al.* demonstrated a stepwise increase in bacterial counts from 10^5 to 10^6 bacteria/L was associated with these symptoms, and considered this to be the early stages of a UTI.[20] (It should be noted that laboratories in certain countries would not use methods that can detect such low numbers of bacteria, as these numbers could be confused with contaminating bacteria).

Dysuria is a common symptom of women with trichomoniasis, and dysuria can also result from vaginal irritation that accompanies candidiasis.

Acute urethral syndrome

In sexually active females with ongoing symptoms, and where uropathogenic bacteria are identified in less than significant numbers, empirical treatment with an antibiotic used to treat cystitis can be considered. If uropathogenic bacteria are not identified, testing for chlamydia, gonococcus, and trichomonas needs to be done; *Mycoplasma genitalium* is also implicated in this condition.[21] The association with chlamydia infection with urethral syndrome in some women can be similar to non-gonococcal urethritis (NGU) in men, and treatment with either doxycycline or azithromycin can bring about resolution of symptoms. Relapses may be due to reinfection from an asymptomatic (male) partner, and referral of such a contact to the STD clinic is essential.

Chronic urethral syndrome

In women with recurrent episodes of urethral syndrome, without an infective cause, alternative strategies are required. Intravaginal administration of topical oestrogens can reduce the frequency of recurrent UTI in post-menopausal women, and may be worthwhile to consider this treatment for chronic urethral syndrome in these patients. A number of anecdotal reports record that diazepam benefits patients because of its anxiolytic effect, and that it is considered to relieve urethral sphincter spasm. The British National Formulary cites a number of preparations for vaginal atrophy, which can be considered in the setting of chronic urethral syndrome, with the comment that treatment, where successful, needs to be reviewed on a regular basis, and that these preparations should be used in the smallest effective amount in order to minimize systemic effects.[22]

Urethritis in the male patient

Organisms	*Neisseria gonorrhoeae* is the cause of gonococcal urethritis (GU), and *Chlamydia trachomatis* is the main cause of NGU; trichomonas, *Mycoplasma genitalium*, and *Ureaplasma urealyticum* are also recognized causes of the condition. The male patient presenting in primary care with dysuria or a frank urethral discharge should have a sexual history taken regarding possible exposure to STI. Ideally, these patients should be seen in a STD clinic where on-site microscopy is done. However, the patient may not wish to do this, and appropriate investigations can be done in primary care. It is important to differentiate between a UTI and urethritis (see below).
Specimen collection	A FCU should be collected, at least 1 hour (preferably 2–4 hours) after the last micturition, in a sterile white-topped plastic container.
Treatment	Doxycycline 100 mg twice daily for 7 days or azithromycin 1 g as a single dose is given for chlamydia. This may not treat gonococcal infection. If the local prevalence of gonococcal infection is high, or if the man is unlikely to return for follow-up, then a single 500 mg dose of ceftriaxone is given intramuscularly.
Complications	Epididymo-orchitis

CHAPTER 4 – *continued*

Vulvovaginitis in pre-pubertal girls

Vulvovaginitis is the commonest gynaecological condition in pre-pubertal girls. The hypo-oestrogenic hormonal milieu is such that there is likely to be increased susceptibility of the vaginal mucosa to infection. Group A streptococcus, *Haemophilus influenzae, Streptococcus pneumoniae* are found on occasion. As gonococcus can multiply on the nonkeratinized vaginal epithelium of pre-pubertal girls, this organism must be considered when there is a suspicion of sexual interference.

Threadworms are a common cause of vulvovaginitis, and should be considered in all children with nocturnal perianal pruritis. Where there are recurrent or persistent symptoms, sexual abuse and STI should be considered. Advice should be sought from the paediatrician.

Foreign bodies are another cause of discharge; the gynaecologist should be consulted. Nonspecific irritation can arise from the use of bubble baths, soaps, poor hygiene, tight clothes, or faecal contamination.

Clinical features	Vaginal discharge, redness, soreness, itching, dysuria, and bleeding (often due to scratching) can be found.
Diagnosis	An introital swab of any discharge should be collected. A swab can also be rolled over the perineal area if inflammation or wet-sticky skin is noted here.
	For threadworm, a few mL of sterile saline should be placed in a sterile universal container. A swab is then moistened in this saline, and repeatedly rolled over the perineal area and gently shaken into the saline 4–6 times. The swab is then cut off into the saline. If the parents are given clear instructions, this can be done in the morning before bathing or defaecating. This may have to be repeated on 4–6 days to exclude the diagnosis.
Treatment	Any growth of one of the three respiratory pathogens cited above should be treated with the appropriate antibiotic.
	Threadworm infection should be treated with mebendazole or piperazine/senna.

Warts

Ano-genital warts represent the commonest sexually-transmitted disease. They are caused by human papilloma viruses (HPV) types 6 and 11, and are transmitted by skin-to-skin contact, which includes vaginal and anal intercourse, as well as the use of shared sex toys. Most infected individuals do not develop visible lesions, and thus transmission can occur when there are no visible lesions. Lesions can appear 2 weeks to several months after an exposure and spontaneous remission of visible lesions occurs in 10–20% of infected individuals. Neoplasia is an uncommon but important complication.

Diagnosis	This is usually clinical; biopsy is uncommonly done. Warts may be confused with the lesions of molluscum contagiosum, but these tend to be found over the pubis, very smooth with a depressed centre from which a cheesy material can be expressed, and unlike warts they are rarely pedunculated.
Treatment	The patient with genital warts should be referred to the STD clinic in order that other STI can be tested.
	Symptomatic discomfort can be relieved by bathing in shallow warm water into which a handful of salt has been dissolved.
	Specific treatment options include:
	Cryotherapy. This is the application of liquid nitrogen directly on the lesions every 1 or 2 weeks until resolution. There can be local ulceration, then healing without scarring in 7–12 days. Success rates range from 50–100%.
	Podophyllin, 10–15% in benzoin tincture, which should not be used on nonkeratinized skin. This is applied directly to soft nonkeratinized warts. In order to protect the surrounding skin, soft paraffin must be applied around the wart first. Podophyllin should be washed off within 6 hours with water. This treatment should be applied with care as toxic neurological, haematological, and febrile complications can arise. If there is no response after applications, an alternative treatment such as bichloroacetic acid (BCA) or trichloroacetic acid (TCA) can be used.
Prevention	Two 'non-live' vaccines against human papilloma viruses are available. These are the bivalent HPV 2 (HPV 16, 18) vaccine (GlaxoSmithKline®) and the quadrivalent HPV 4 (HPV 6, 11, 16, 18) vaccine (Merck & Co, Inc®). Both are recommended for the prevention of cervical cancers and precancers, and HPV 4 is also recommended for prevention of genital warts.[23]

CHAPTER 5

A description of important conditions and organisms associated with skin and soft tissue infections in primary care for general information.

Acute paronychia	
Organisms	*Staphylococcus aureus* (MSSA and MRSA) Other bacteria include group A streptococcus, pseudomonas and 'coliforms'. Infection in thumb-sucking or nail biting children can involve oral anaerobes. (Chronic paronychia is often caused by candida, in the setting of frequent exposure to water; see Chapter 6). Herpetic whitlow should also be considered.
Specimen collection	Many infections settle spontaneously. Swabbing inflamed skin is of no use, but a swab should be collected when an incision and drainage are done. Where herpes is likely, this can be confirmed by carefully opening the lesion, taking up the fluid on a dry swab which is cut into VTM, or a dry swab and examined for HSV by PCR (see Chapter 9). Staphylococcal whitlow is a deeper infection of the distal phalanx of a finger or toe. If facilities are available in primary care, a fluctuant whitlow should be incised and drained, and a wound swab of any pus collected.
Treatment	Flucloxacillin or a macrolide can be given. If there is no response to treatment after 2 days, co-amoxiclav can be prescribed. This will widen the cover to include 'coliforms' and anaerobes. For suspected staphylococcal whitlow, empirical treatment with oral antibiotics is needed. The affected limb should be elevated, and warm soaks applied 3–4 times a day. If the risk factor is frequent wet hands, candida should be considered. Topical treatment can be effective for localized infection confined to the nail fold, and amorolfine (twice weekly) or tioconazole (twice daily) for up to 6 months can be used. For more severe infection, oral treatment that can be used is itraconazole 200 mg q12h for 7 days of three 28-day cycles. Waterproof gloves should be used to eliminate the risk (see Chapter 6). Analgesia should be given.
Complications	If there is cellulitis, lymphangitis, and ongoing fever, referral to hospital is required.

CHAPTER 5 – *continued*

Bites – Animal

'Risks'	Serious infection can occur in otherwise healthy individuals; wounds to the hands, those that are likely to involve joints, tendons, ligaments or bone, as well as puncture wounds and crush wounds, all require particular attention. Individuals who are elderly, diabetic, immunocompromised, splenectomized, or have liver disease are at risk of serious infection from bite wounds in general, as are females bitten or scratched on the hand or arm on the side of a mastectomy, where there is poor lymphatic drainage, and resulting lymphoedema. All these individuals should be referred to hospital promptly.
Organisms	A wide range of bacteria can be involved, and include members of the animal oral flora such as *Pasteurella multocida*, *Eikinella corrodens*, and *Capnocytophaga canimoris*. *Staphylococcus aureus* and anaerobes are also important.[12–14] *Bartonella henselae* is the causative agent of 'cat-scratch' disease (CSD). This should probably be called 'kitten-scratch', as kittens are often bacteraemic with this organism. Children can be scratched when cuddling a kitten on the shoulder, and an inoculation papule develops, with subsequent erythema nodosum and cervical lymphadenopathy which resolves over several months. (CSD can be diagnosed serologically; when treatment is required azithromycin 500 mg day 1 and then 250 mg days 2–5 can be given.) Bites from pets such as turtles and terrapins can be associated with *Mycobacterium marinum*. (In the patient with a chronic infection of the joints of the hands, it is essential to ask them if they keep tropical fish, as *Mycobacterium marinum* resides in fish tanks. Failure to ask the question can miss the diagnosis, leading to months of inappropriate courses of antibiotics, and the potential for disseminated infection in the immunocompromised individual.)[15] Rabies must always be considered, especially where the bite has occurred in an endemic area of the world (see below).
Management	Patients with 'at risk' animal bites should usually be referred to hospital. If possible, it is worthwhile to take photographs, or make a clear drawing of the affected area. Bite wounds that are less than 8 hours old will be *contaminated* with a range of bacteria. Those over 8 hours will be likely to have *established infection*, and pus may be present or expressed for wound swab collection. Because of complications that can occur in bites to the hand and face, prompt referral to hospital should be considered in all but the most superficial of infections at these sites. Copious amounts of sterile saline should be used to irrigate wounds, and for puncture wounds a saline jet using a 20 mL syringe and 18 or 19-gauge needle should be used. Nonviable tissue is debrided.
Prophylaxis	For wounds less than 8 hours old, individuals in the 'risk' groups (above) at least should have prophylactic antibiotic for 7 days; co-amoxiclav is a suitable option. Patients must be reviewed within 48 hours.
Treatment	For wounds more than 8 hours old, individuals in the 'risk' groups (above) at least should have antibiotic treatment for 7 days; co-amoxiclav is a suitable option. For the penicillin-allergic patient, metronidazole and doxycycline or clindamycin and ciprofloxacin/levofloxacin can be given. The medical microbiologist should be contacted for advice, particularly regarding the penicillin-allergic child. Elevation and rest of an affected limb, and hand/arm in particular is very important. Failure to do this is a likely cause of treatment failure. Patients must be reviewed at 24 and 48 hours after the first visit.
Tetanus	Tetanus prophylaxis compatible with patient's vaccination status must be given.
Rabies	If the patient has sustained a bite from an animal in an endemic area, it is important to contact the relevant public health officer immediately. Helplines are available 24/7. Essential information about the bite to relay includes: Date, country and place, site of bite on the body, description of the bite, the type of animal and its behaviour at the time of the incident, follow-up information on the animal. For example, has examination of the brain shown histological evidence of rabies infection? Details of any rabies prophylaxis given in the country where the bite took place should be ascertained. Contact numbers: In the UK, these are documented in the *British National Formulary*.

Bites – Human

'Risks'	Human bites have a higher complication and infection rate than animal bites. Serious infections can occur in the hands, often associated with 'clench fist' on the part of an aggressor. 'Love nips' to the breasts and genitals can also lead to serious infection. A particular problem is the late presentation of many of these cases, 24–48 hours after the incident, when infection is established.
Organisms	A wide range of bacteria can be involved, and include members of the human oral flora such as peptostreptococci, *Streptococcus anginosis*, haemophilus, fusobacterium, and *Eikinella corrodens*.[14] HBV and HIV should always be considered.[16] Immediate referral to the STD clinic or local emergency department must be made.
Management	It is worthwhile to take photographs or make clear drawings of the affected area. Individuals with human bite wounds often present late. Swabs should be collected, and then copious amounts of sterile saline should be used to irrigate wounds, and for deep/puncture wounds a saline jet using a 20 mL syringe and 18- or 19-gauge needle should be used. Nonviable tissue needs to be debrided. Those with hand wounds must be referred to a hand surgeon as soon as possible for full evaluation and management.
Prophylaxis	Antibiotic prophylaxis is given for patients with uninfected wounds, usually co-amoxiclav for 7 days. For the penicillin-allergic patient, metronidazole and clarithromycin or clindamycin and ciprofloxacin can be given for 7 days. Prophylaxis for HBV and HIV must be considered (a risk assessment of the 'donor' for these viruses should be done, and if possible a blood sample collected for testing; see Chapter 9). A 'baseline' blood from the 'recipient' should be collected for long-term storage, and a rapid course of HBV vaccine initiated. As presentation often occurs many hours after injury, the role of HIV prophylaxis needs to be reviewed with the experienced officer in the locality, such as the STD and infectious diseases physician.
Treatment	The antibiotic of choice is co-amoxiclav for 7 days. For the allergic patient, metronidazole and clarithromycin can be given; the medical microbiologist should be contacted for advice. Elevation and rest of an affected limb, and hand/arm in particular is very important. Failure to do this is a likely cause of failure. Patients must be reviewed 24 and 48 hours after the first visit.
Tetanus	Tetanus prophylaxis compatible with patient's vaccination status must be given.

Boils and carbuncles

Organisms	*Staphylococcus aureus* (MSSA and MRSA), including PVL-producing isolates.
Specimen collection	Swabs should be sent if there is pus to collect; swabs of inflamed skin are unhelpful.
Treatment	Fluctuant lesions should be incised and drained, and covered with a sterile dressing. Antibiotics should be given if there is fever and/or cellulitis, the lesion is large (a carbuncle), or on the face; flucloxacillin or erythromycin are suitable for MSSA. Large nonfluctuant lesions should have moist heat applied at least four times a day. A clean hand-towel should be dampened with boiled water on a clean surface, and when cooled sufficiently to hold, pressed against the lesion for 5–10 minutes; antibiotics should be given. Paracetamol or ibuprofen can be given for analgesia.
Complications	Depending on the site, complications include scarring, cellulitis, thrombophlebitis, septic arthritis, septicaemia, and endocarditis. Although rare, cavernous sinus thrombosis is a complication of boils and carbuncles on the upper lip and cheek. In the setting of recurrent boils a wound swab should be collected, and 5 days of the MRSA decolonization procedure used (this is effective for both MRSA and MSSA). A nose swab can also be collected if there are no other isolates; here the request form should be clearly marked for the attention of the medical microbiologist, who should also be contacted directly. Relevant isolates will be sent to the reference laboratory for PVL toxin gene testing.

CHAPTER 5 – *continued*

Cellulitis

Organisms	*Staphylococcus aureus* (MSSA and MRSA), including community-acquired MRSA in the USA.
	Group A streptococcus (occasionally group C and G streptococcus)
Other groups:	<3 months of age; group B streptococcus
	Perianal/introital cellulitis in young girl; group A and group C streptococcus
	Balanitis in boys; group A streptococcus
	Cellulitis following water exposure (often involves gram-negative organisms; vibrios; aeromonas); seek the advice of the medical microbiologist.
	(Cellulitis associated with animal and human bites, see separate sections).
Specimen collection	Swabs of intact skin are of no value, as normal skin flora will be present. Swabs can be useful if there is broken skin or blisters (which can also be aspirated), or where there is an obvious portal of entry. Pus may occasionally be present.
Treatment	For MSSA, flucloxacillin or clarithromycin can be used. Clindamycin can also be used in the penicillin-allergic patient, and is more effective than erythromycin. This antibiotic should be used with caution in the older patient, particularly the malnourished and immunocompromised, as there is a higher risk of CDAD. When *Staphylococcus aureus* is reported as erythromycin sensitive, it is clindamycin sensitive.
	If MRSA is a consideration, empirical antibiotics should be based on local prescribing guidelines and prevalence information. Doxycycline and rifampicin are examples of an antibiotic combination that can be used.
	An analgesic should be prescribed. Where possible, bed rest, elevation, and ankle exercises of the affected limb should be done. Portals of entry such as 'athlete's foot' or chronic leg ulcers should be treated. Long-term plans to manage ulcers should be planned with the tissue viability nurse, in order to prevent recurrent cellulitis. It is essential to mark any area of cellulitis with a skin marker, or take a picture, so that spread can be monitored. Moderate to severe cellulitis requires immediate assessment for hospital admission and intravenous antibiotics.
Complications	Extension of infection, bacteraemia, septic shock. Necrotizing fasciitis is a surgical emergency and should be suspected when there is severe pain or a dusky purple appearance impending gangrene of the tissues.

Chronic leg ulcers

Organisms	*Staphylococcus aureus* (MSSA and MRSA) Group A streptococcus Group C, G streptococcus
Specimen collection	Only consider swabbing if there is clinical evidence of infection such as pain, erythema, swelling, enlargement of the ulcer, and/or surrounding cellulitis, with or without fever. As shown in **90**, the way the swab is collected is important. Taking into consideration discomfort for the patient, sterile gauze or a swab can be used to remove as much slough as possible, and a second swab is rolled deeper around viable tissue for sampling.
Treatment	The condition of the ulcer should always be reviewed. In order to reduce infection, the 'critical colonization' stage should be minimized with regular washing. A litre of water can be boiled, and one heaped tablespoon of aqueous cream mixed into this once this water has cooled. The use of aqueous cream is important as it moistens the surrounding skin; dry scaly skin is more likely to be colonized with *Staphylococcus aureus.* Compression bandages should not be used if there is evidences of cellulitis. Dressings should be reapplied daily or on alternate days to allow full assessment. Topical antibiotics should generally not be used; variable penetration of the agent will select for resistant bacteria. They can also sensitize the patient to the antibiotic. Topical metronidazole can be used. Use flucloxacillin or a macrolide. (Clindamycin can also be used in the penicillin-allergic patient, and is more effective than erythromycin. This antibiotic should be used with caution in the older patient, particularly the malnourished and immunocompromised, as there is a higher risk of CDAD). If MRSA is a consideration, empirical antibiotics should be based on local prescribing guidelines and antibiotic susceptibility data. Doxycycline and rifampicin is a combination of antibiotics that can be used.
Complications	Bacteraemia and sepsis, especially in the setting of cellulitis. The major complication of diabetic foot ulcers is osteomyelitis.

Folliculitis

Organisms	*Staphylococcus aureus* (MSSA and MRSA), *Pseudomonas aeruginosa* (hot-tub folliculitis).
Specimen collection	Swabs should only be collected in cases of recurrent or chronic folliculitis, in order to determine the identity of the causative organism and its antibiotic susceptibility pattern. If hot-tub folliculitis is suspected a specimen should be collected from a pustular lesion.
Treatment	Daily washing with an antiseptic product can prevent and treat mild staphylococcal folliculitis; topical fusidic acid can also be applied. Severe infection should be treated with an oral antibiotic; flucloxacillin or clarithromycin can be used. Tight clothing and occlusive dressings over affected areas should not be used. When shaving, shave in the direction of hair growth. Similarly application of moisturizing lotions or gels should be in the direction of hair growth.
Complications	Scarring can occur with recurrent and chronic infection. With hot-tub folliculitis, pseudomonas is the likely organism and can be grown from the lesions. A hot-tub/jacuzzi that is inadequately cleaned/maintained/disinfected allows the proliferation of pseudomonas in the water (water samples can be taken to isolate the organism). The jets push the water, and pseudomonas into dilated skin pores, giving rise to the folliculitis. The local public health department must be informed. The hot-tub/jacuzzi should be taken out of use until it is properly decontaminated, and a procedure for maintaining safety is in place.

CHAPTER 5 – *continued*

Impetigo

Organisms	*Staphylococcus aureus* (MSSA and MRSA) Group A streptococcus Impetigo is a contagious infection of the superficial layers of the skin, usually starting with thin-walled vesicles that rupture, then crusts. Bullous impetigo is characterized by the formation of large blisters in intact skin. The infection can arise by direct invasion, or secondary to other conditions, such as eczema, scabies, or trauma.
Specimen collection	The diagnosis is clinical, and swabs should only be sent if there is no response to treatment, the infection is severe and extensive, or is recurrent. With facial impetigo, nasal swabs will often confirm carriage of MSSA or MRSA.
Treatment	General hygiene measures, such as regular washing, and drying with a clean towel may be adequate for mild impetigo. Topical fusidic acid q8h can be used for small lesions not exceeding 1–2 cm in diameter. Mupirocin should be reserved for MRSA, in order to reduce the pressure to select resistant organisms. Retapamulin is also active against *Staphylococcus aureus* and streptococci. For more widespread infection, flucloxacillin or a macrolide is used. Skin care is the centre of management, and should be started before topical antibiotics are applied. The lesions should be softened in warm soapy water, rinsed in warm water, and carefully dried with a clean towel. Hands should be washed after touching lesions. Towels, clothing, and bedclothes should not be shared and should be changed regularly. The use of chlorhexidine baths or showers (see MRSA) has not shown any advantage. Infected individuals in 'high-risk' settings such as nurseries should not be allowed to return until lesions have crusted over, or they have had 48 hours of antibiotics.
Complications	These include spread to other parts of the body, scarring, and spread to other individuals. Cellulitis, lymphadenitis, abscess formation, and staphylococcal scalded skin syndrome or toxic shock can occur.

Methicillin-resistant *Staphylococcus aureus* (MRSA)[17]

What is MRSA?	MRSA is a variant of *Staphylococcus aureus* which is resistant to almost all penicillins (flucloxacillin), cephalosporins, and carbapenems. The term MRSA is confusing and arose because when testing sensitivity of *Staphylococcus aureus* to beta-lactams (i.e. flucloxacillin dicloxacillin), the laboratory used methicillin, as this was more reliable than testing individual penicillins and cephalosporins.
Is it more likely to give rise to infection?	In general, MRSA is no more pathogenic than a MSSA, i.e. MRSA does not cause infections over and above those expected of a sensitive *Staphylococcus aureus*. However it is important to minimize its prevalence, and clinical impact, and prevent occurrence in MRSA-free areas.[18] In the UK, the prevalence of MRSA in those living at home is <1%, rising to more than 22% in care home residents.[19, 20] MRSA-colonized patients are at risk of developing infection by the strain of MRSA they are colonized with. Of concern is the emergence in the last decade of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) in patients without health-care contact, both in the USA and Europe.[21, 22] In the UK and USA, national guidelines have been produced for the management of CA-MRSA.[23, 24] As with MSSA, isolates of MRSA that produce the PVL toxin, a virulence factor, are increasingly prevalent in the community, and recognition of infections where these organisms may be implicated is important (see PVL below). In the USA, there is increasing concern of one clone of CA-PVL-MRSA (USA300), which is now spreading to hospitals.[25]

(*Continued*)

Methicillin-resistant *Staphylococcus aureus* (MRSA)[17] *continued*

Can infections be treated?	There are a number of effective antibiotics available for the treatment of MRSA infections that can be administered either orally or parenterally. What should the primary care physician do if a patient is found to have MRSA? The patient may be found to be MRSA positive either following submission of a clinical specimen or as a result of a MRSA screen. The clinical specimen that is positive for MRSA: 1. Is there any clinical evidence of infection? If taken from a nonsterile site and there is no clinical evidence of infection then systemic antibiotics are not indicated. Most patients are colonized rather than infected. 2. Is the patient due to undergo a procedure or be referred to a health-care provider? It is important that the MRSA status is communicated to other health-care professionals providing treatment. The appropriate infection control precautions can then be taken, MRSA decontamination protocols used as necessary, and the appropriate prophylactic antibiotics given, when indicated. 3. Ensure that the positive MRSA status of the patient is recorded in the patient's notes so that if any other staff member sees the patient they are then made aware of this. 4. Inform MRSA-positive patients of their status and provide them with the necessary advice and a factual information leaflet about the organism. If patients require medical consultation or treatment in the future, they should be told to inform staff caring for them immediately of their MRSA status. 5. Consider whether the patient should receive a course of topical decontamination (see below). 6. If the patient is a HCW, or comes into contact with other vulnerable patients, they must inform their occupational health department prior to returning to work. 7. If another member of the household is a patient who works in the health-care setting then they should inform their occupational health department.
Treatment	Prior to initiating any treatment a decision needs to be made as to whether the site from which the specimen was collected shows evidence of infection. Most MRSA isolates reflect colonization and do not require systemic antibiotic therapy. However, where there is evidence of infection then antibiotics are indicated. MRSA are resistant to the majority of penicillins and cephalosporins. The activity of other antibiotics varies. Thus it is important to be guided by local sensitivity patterns. Recognized antibiotic combinations for sensitive isolates, include doxycycline or trimethoprim with either rifampicin or fusidic acid (rifampicin and fusidic acid should not be used together because of the risk of jaundice). Linezolid is another oral agent that can be used, but requires weekly monitoring of the FBC, and within the UK is not licensed to use for longer than 1 month. Nitrofurantoin can be used to treat lower UTI caused by MRSA.
MRSA screening	MRSA screening prior to hospital admission is recognized as being increasingly important, and by 2011, all patients admitted to UK hospitals will need to be screened either prior to admission for elective procedures, or on arrival at the emergency department. Please refer to local guidelines. Primary care practices/clinics may be involved in elective pre-admission screening. This should be done as close to the date of admission as possible, and schedules are set by local guidelines. Screening process: See local guidelines. In general when taking a swab, this should be pre-moistened in sterile water or saline to improve 'loading' of the swab.
MRSA reporting	The results issued will either be 'MRSA ISOLATED' or 'MRSA NOT isolated'. Although done on the first positive screen, antibiotic susceptibility profiles are often not reported on subsequent screening swabs.
MRSA suppression	Topical antiseptic washes together with nasal ointment are used in an attempt to 'eradicate colonization'. The more realistic view of eradication is that MRSA carriage is suppressed below the levels of detection as judged by screening. This fine balance may be upset in the future by for example the prescription of an antibiotic that suppresses the normal flora thus allowing MRSA to 'fill the void'. From a practical perspective, once a patient has been found to be MRSA positive they should always be regarded as being potentially positive in the future even if they have had a set of negative screening swabs.

(*Continued*)

CHAPTER 5 – *continued*

Methicillin-resistant *Staphylococcus aureus* (MRSA)[17] *continued*

When to attempt decolonization:

- Anyone who is found to be positive should undergo at least one course of decolonization. This is not only to reduce risk to the individual but also an attempt to reduce the incidence of MRSA within the community.
- Prior to any procedure where there is a risk of MRSA causing an infection. Within the UK this has been extended to virtually any procedure despite the fact that there may be little or no risk to the individual.

MRSA suppression is not always effective especially in the individual with a chronic skin condition, carriage in the respiratory tract other than the anterior nares, or if urine is colonized in the long-term catheterized patient.

Role of the primary care physician:

- You may be asked to prescribe the MRSA suppression regimen and take follow-up swabs or undertake the initial screen. The patient should also be given an instruction sheet on how to carry out the decontamination. For some individuals, especially the elderly, certain steps will be difficult for them to perform without help, such as washing linen and undergarments every day from the beginning of the process.
- Occasionally, a patient whose MRSA suppression is ineffective despite repeated cycles of decolonization, is blocked from having a procedure by the surgical team. If this occurs then the case should be discussed with the clinician and microbiologist (see below.).

What should be done if MRSA suppression has been ineffective?

For patients awaiting successful suppression prior to a procedure and negative swabs cannot be achieved after a maximum of three attempts a decision needs to be made about whether to go ahead with the procedure. The patient and consultant in charge of the case (with some input from the microbiologist) should be involved in making the decision. Any risk can be minimized by starting the patient on suppressive therapy 4 days before the procedure and continuing this until after the operation. Where indicated, perioperative antibiotic prophylaxis should include an agent active against MRSA.

MRSA suppression protocols

These will vary but essentially suppression of MRSA is achieved by reducing nasal and skin carriage. Usually this is given for 5 days, and 2 days later the patient is rescreened for MRSA.

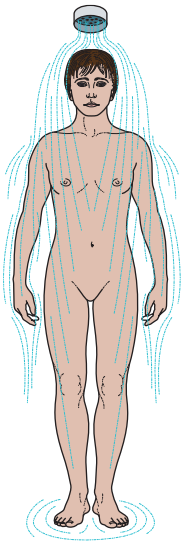
Nasal carriage: Liberally apply a pea-sized amount of mupirocin to each nostril as far as the small finger will comfortably allow, three times a day. The patient should 'taste' the mupirocin at the back of the throat. If the isolate is mupirocin resistant then alternative agents should be used.

Skin carriage: Preferably showering, or bathing, the patient should use one sachet of 2% tricolosan as the shampoo and soap, cleaning the hair, hair line, axillae, and groin/perineal areas well. A 4% chlorhexidine gluconate shampoo/body wash can be used as an alternative. Octenisan®, which contains the active antiseptic ingredient octenidine, is also available. A cartoon to show patients how to perform the body wash is shown (**181**).

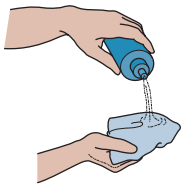
Post-suppression screening should be guided by local community and hospital infection control guidelines.

181

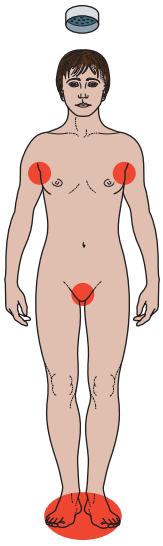
Ensure all skin surfaces are covered with the body wash.



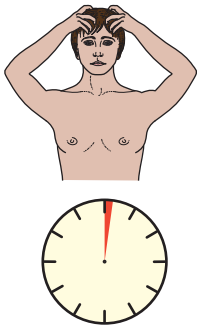
Ensure that your hair and body are wet



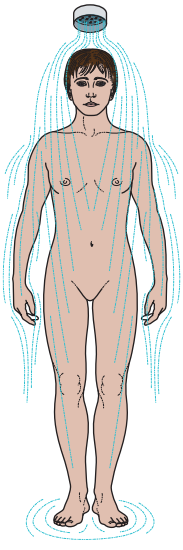
Put the lotion onto a damp disposable washcloth



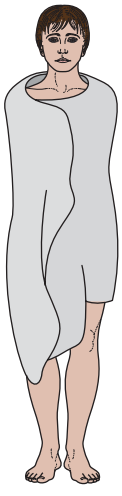
Apply all over hair and body paying special attention to the areas indicated in red



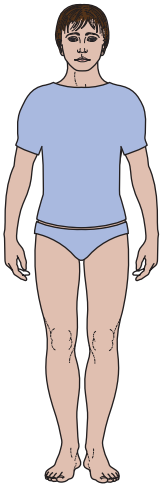
Leave the lotion on your skin for one minute before rinsing



Rinse off thoroughly



Dry with clean, dry towel



Put on clean underclothes/ nightwear every day
Ensure all bed linen is changed daily

181 Patient leaflet showing 5-day antimicrobial wash procedures.

CHAPTER 5 – *continued*

Panton–Valentine leucocidin (PVL) *Staphylococcus aureus*[26]

PVL is an important virulence factor of certain strains of *Staphylococcus aureus*, both MSSA and MRSA. The PVL marker is strongly associated epidemiologically with transmissible, virulent, strains of *Staphylococcus aureus*. In the USA, community-associated (CA) MRSA is a recognized entity, associated with severe soft tissue infection and necrotizing pneumonia in otherwise healthy young people. About 2% of *Staphylococcus aureus* isolates are PVL producers.[27] Detailed guidelines have been produced in the UK.[28]

Clinical features	Skin and soft tissue infections are often recurrent, and include boils, carbuncles, folliculitis, cellulitis, and purulent eyelid infections. The pain and erythema can be out of proportion to the severity of cutaneous findings, and necrosis can be present. Necrotizing pneumonia, necrotizing fasciitis, pyomyositis, septic arthritis, and osteomyelitis are examples of invasive infections.
Risk factors	Risk factors where there is a higher chance of transmission have been identified, and these include households, close contact sports, military training camps, gyms, and prisons. Pets such as dogs can also be a source. The '5 Cs' are:[28] • Contaminated shared items, e.g. towels, razors. • Close contact. • Crowding. • Cleanliness (poor hygiene). • Cuts and compromised skin integrity.
Diagnosis	Diagnosis of PVL MSSA or MRSA requires isolation of the organism, following which it is sent to the reference laboratory to identify the presence of the genes that code for PVL. Staphylococcal isolates are not routinely tested for PVL genes. It is essential that the physician requests the laboratory to send the isolate for PVL testing when the clinical features indicate that a PVL strain may be responsible. It is worthwhile to note any severe soft tissue infections in otherwise healthy individuals, especially where there are clusters of disease associated with close contacts. Public health should be informed.
Treatment	The Antibiotic Guidelines (Chapter 11) should be referred to, and the medical microbiologist can be contacted for advice. Leaking or draining skin lesions should be covered. Isolates in the USA are usually sensitive to clindamycin, which can be given at a dose of 450 mg q6h, noting that there is a risk of CDAD.
General advice	After skin lesions have dried, decolonization protocols discussed above for MRSA can be used. It is important that general hygiene is discussed with the patient. Sheets, body-, face-, hand-towels should not be shared, should be changed daily, and washed at the highest temperature cycle permitted by the fabric in a washing machine. Clothes including underwear should be changed daily and washed likewise. Pump action soap dispensers should be used; with bars of soap there is a risk of cross-infection. Wash basins, baths, and showers should be cleaned with a household detergent using disposable cloths. Rooms, especially the bedrooms, should be cleaned daily, including vacuuming.

CHAPTER 6

Some general information of common fungal infections found in the community[3, 4]

'Athlete's foot' (tinea pedis)

Organisms	*Trichophyton rubrum*, *Trichophyton mentagrophytes* var. *interdigitale*, *Epidermophyton floccosum*
Source	Swimming pools and other communal areas where the skin between the toes remains wet or damp for long periods. Some individuals in a family may have repeated infections, while others are never affected.
Symptoms and signs	Scaling, painful fissuring with occasional bleeding, and maceration affecting the fourth and fifth toes first. The infection can then spread to the other toes, the lateral aspects of the foot, with dry scaling and vesicles/bullae. The associated pruritis can be very distressing for the patient. There is often an associated infection in the groin (tinea inguinum), which requires simultaneous treatment.
Diagnosis	The clinical presentation is usually obvious, but skin scrapings can be taken, especially if the patient is immunocompromised.
Treatment	Topical agents include terbinafine, clotrimazole, econazole, ketoconazole, and miconazole, as well as undecenoates. Ether-based 'cooling sprays' are very useful in relieving the significant discomfort of the condition. Oral terbinafine, 250 mg/day for 2–4 weeks, or itraconazole 200 mg q12h for 7 days, can be used when the response to topical treatment is inadequate. Topical treatment should also continue for 8 weeks or longer. In addition, the patient must wash and dry the feet daily, preferably using fresh towels. The groin area should also be carefully dried after bathing; towels should not be shared with other family members. A hair dryer, on low heat, can be used to dry the feet and groin area after bathing. Clean cotton socks should be changed daily, and shoes alternated every 2 days or so, and allowed to dry before reuse. In the house, showers and baths should be cleaned at least weekly with a strong household bleach to decontaminate the area, which should then be dried.
Complications	Spread to the groin. Secondary bacterial or candida infection. Cellulitis with group A, C, or G streptococcus. These bacteria can use the fissures as the portal of entry. The feet should always be checked for athlete's foot when there is cellulitis.

Chronic paronychia

Organisms	*Candida albicans* (with secondary infection by *Staphylococcus aureus* or *Pseudomonas aeruginosa*).
Symptoms and signs	This is a common disorder, usually found in women between the ages of 30 and 60 years. The most important factor is repeated exposure to water. The thumb and index finger are usually involved. The infection starts with a slight swelling of the proximal nail fold, and discharge of pus. Once the cuticle is damaged, water, bacteria, and irritants all cause problems.
Diagnosis	Collect pus for culture of both yeasts and bacteria. (The differential diagnosis can include herpetic whitlow; here fever, lymphadenitis, and axillary lymphadenopathy occur. A swab for HSV PCR can be collected.)
Treatment	Topical treatment can be effective for localized infection confined to the nail fold, and amorolfine (twice weekly) or tioconazole (twice daily) for up to 6 months can be used. For more severe infection, oral treatment that can be used is itraconazole 200 mg q12h for 7 days of three 28-day cycles. Resolution of the condition can be prolonged, and also centres on the reducing exposure to moisture and irritants. The use of waterproof gloves, careful handwashing and drying, and in the evening, the application of skin ointment. For difficult cases, washable cotton gloves can be worn under impermeable gloves.

CHAPTER 6 – *continued*

Groin infection (tinea inguinum)

Organisms	*Trichophyton rubrum*, *Epidermophyton floccosum*
Symptoms and signs	Bilateral, often purple papular lesions along the line of the inguinal ligament. Pruritis can be significant and distressing. Many patients have concurrent 'athelete's foot' infection.
Diagnosis	The clinical presentation is usually obvious, but skin scrapings can be taken if the diagnosis is uncertain, especially in the immunocompromised patient.
Treatment	Topical agents include terbinafine, clotrimazole, econazole, ketoconazole, and miconazole, as well as undecenoates. Oral terbinafine, 250 mg/day for 2–4 weeks, or itraconazole 200 mg q12h for 7 days, can be used when the response to topical treatment is inadequate. Topical treatment to the groin (and toes) should continue. In addition, the patient must wash and dry the groin region daily, preferably using fresh towels. The feet should also be carefully dried after bathing; towels should not be shared with other family members. A hair dryer, on low heat, can be used to dry the feet and groin area after bathing. Loose-fitting, clean cotton underwear should be changed daily, and shoes alternated every 2 days or so, and allowed to dry before reuse.

Onychomycosis (tinea unguium)

Organisms	*Trichophyton rubrum* is the commonest cause of nail infection. *Scopulariopsis brevicaulis* can be a relatively common secondary invader of the damaged nail. *Trichophyton mentagrophytes* var. *interdigitale* is also associated with superficial white onychomycosis.
Symptoms and signs	About 20–30% of adults over the age of 40 years have fungal nail infections, usually of the toe nails. Distal subungual infection, with penetration of the hyponychium and extension along the ventral surface of the nail, causing nail lysis, cracking and crumbling. The entire nail can be involved. Proximal infection occurs with involvement of the proximal nail fold, leading to damage of the growing nail, with severe deformation and ridging.
Diagnosis	Nail clippings and nail scrapping with subungual debris must be collected to identify the organism, and confirm the infection. For superficial white onychomycosis, scrapings of the nails surface should be taken.
Treatment	Treatment of nail infection is long-term, and there must be enough time for the nail to grow out before treatment can be considered successful. Toe nails take 12 months and finger nails 6 months to grow out. Topical antifungal nail polish can be used for very mild disease. Long-term systemic agents are required to achieve therapeutic levels, and include terbinafine and itraconazole. Terbinafine, 250 mg/day for 6–12 weeks (fingers) and 3–6 months (toes), or itraconazole 200 mg q12h for the first 7 days of two 28-day cycles for fingers, or three 28-day cycles for toes. Recurrence occurs and cure may be difficult (patients need to appreciate that cure is not always possible). Reinfection from shoes, the environment, and other individuals occurs. Overlapping and tightly compressed toes may be predisposing factors. As *Scopulariopsis brevicaulis* is a secondary invader of damaged nails, treatment of an underlying dermatophyte infection may often resolve the condition. Itraconazole may be effective, but often the only effective treatment is nail softening with 40% urea, under occlusion, for a week, followed by nail removal.

Pityriasis versicolor

Organism	This infection is caused by lipophilic yeasts of the genus *Malassezia*. These fungi are members of the normal flora of the skin, and most infections are endogenous in origin. The incidence of colonization is about 25% in children, and up to 100% in adults. It is likely that colonization is established at the time of puberty, when the sebaceous glands become active. The increased incidence of infection in the immunocompromised, for example HIV/AIDS, or patients on steroids or other immunosuppressive treatment implies a relationship between the immune system and the infection. The infection, while disfiguring, is otherwise harmless.
Symptoms and signs	Characteristically, there are patches of fine brown scaling, especially over the trunk, neck, and upper arms. The disease is exacerbated by sunlight and sweating. In immunocompromised patients, the lesions can be more erythematous, and can feel raised.
Diagnosis	Microscopy is done to make the diagnosis. Scrapings should be taken from affected areas of skin. Clusters of round or oval budding yeast cells and short hyphae are sufficient to confirm the diagnosis. The yeast does not grow in routine culture in the laboratory
Treatment	When left untreated, the infection persists for long periods. While response to topical treatment is usually good, relapses, not surprisingly, occur. Topical imidazoles such as clotrimazole, miconazole, or econazole should be applied in the morning and evening for 4–6 weeks. For extensive infection, or those that do not respond satisfactorily to topical therapy, itraconazole (200 mg/day for 1 week), or ketoconazole (200 mg/day for 1 week) can be given. Terbinafine and griseofulvin are not effective.

CHAPTER 6 – *continued*

Scalp infection – ringworm (tinea capitis)

Organisms	*Trichophyton tonsurans* and *Microsporum canis.* Spread is usually person-to-person in the home and school setting in particular, or acquired from cats and dogs. The spores remain viable for long periods on hair combs and brushes, furniture, and bed sheets. The infection mainly occurs in pre-pubertal children, and is more common in boys than girls. Disease is uncommon after the age of 16 years. Asymptomatic carriage can occur in adults and older children.
Symptoms and signs	Discrete circular patches of hair loss, with scaling of the skin. The lesions may be tender and boggy, and in severe case, there can be fever and lymphadenopathy. The florid form is known as 'kerion', a painful inflamed mass with crusting and pus-like material, which can be confused with a bacterial abscess. The longer this remains undiagnosed, the more likely are complications such as scarring and alopecia.
Diagnosis	While the clinical presentation is usually obvious, skin scrapings and several pulled hairs must be collected. Scalp infection may be so common, that it should be considered in any child over 3 months with a scaly scalp.
Treatment	Local specialist advice from the dermatologist should be used to determine guidelines. Systemic treatment is required, as topical agents are unable to penetrate the scalp effectively. Where there is no response to terbinafine, griseofulvin can be used as it is considered to have better activity against the less common agent of the condition, *Microsporum canis.* Although there is no evidence for efficacy, the use of antifungal shampoos for the whole family can be considered for the duration of treatment.
Children:	Griseofulvin: 10 mg/kg/day for 6–8 weeks increased to 20 mg/kg/day if failure to respond at 6 weeks or *Trichophyton tonsurans* has been isolated. *Microsporum canis* may require 12 weeks treatment. If the patient fails to respond to treatment, or the side-effects necessitate discontinuation, terbinafine can be considered. Terbinafine: (not licensed for children): 62.5 mg/day child <20 kg, 125 mg/day 20–40 kg, 250 mg/day >40 kg. To be given for 4 weeks at least, but longer for *Microsporum canis* infection, as treatment may be less effective for this dermatophyte.
Adult	Terbinafine: 250 mg/day for at least 4 weeks.
Complications	Secondary bacterial infection, or candidiasis, hair loss, and scarring (see 'kerion' above).
Public health	If there are two or more children in a class with the infection, the remainder of the class should be screened following parental consent. The local public health authority would manage this situation. It should be pointed out that the disease is treatable, and is not a sign of neglect. There is no need to miss school (or work), as the infection is likely to have spread by the time of diagnosis. While treatment reduces the risk of transmission, any risks of transmission should be minimized by avoiding contact sports. Sharing of combs, brushes, and hats should be avoided. If a pet is the likely source, the animal should have a veterinary inspection.

Skin infection – ringworm (tinea corporis)

Organisms	*Epidermophyton floccosum*, *Microsporum canis*, *Trichophyton rubrum*, *Trichophyton tonsurans*, *Trichophyton verrucosum.* Spread is from infected humans and animals such as cats and dogs. The spores remain viable for long periods on hair combs and brushes, furniture, and bed sheets.
Symptoms and signs	On the trunk and limbs, there can be single or multiple scaly, circular erythematous plaques with a raised advancing border. There may be varying degrees of inflammation, with pustules on the border.
Diagnosis	The clinical presentation can be obvious, but skin scrapings should be collected if the diagnosis is uncertain, the infection is refractory to empirical treatment, or when oral treatment is being considered. Material should be collected from the raised border of the lesion by scraping outwards with a blade held perpendicular to the skin.
Treatment	Topical agents include terbinafine, clotrimazole, econazole, ketoconazole, and miconazole, as well as undecenoates. Oral terbinafine, 250 mg/day for 2 weeks, or itraconazole 100 mg/day for 2 weeks, can be used when the response to topical treatment is inadequate.

CHAPTER 7

This is a summary of the material in the report by Working Group of the former PHLS Advisory Committee on Gastrointestinal Infections.[16] This information is included here for general information only, as the guidance is for UK public health and environmental health officers.

For each organism, the usual source, incubation period, symptoms, treatment, and public health issues are summarized. See **105** for risk groups. Notification responsibilities are given in Chapter 1.

F/O: faecal–oral route of transmission. (Reproduced with permission of the UK Health Protection Agency)

Amoebiasis (*Entamoeba histolytica*)

Source:	F/O, water, food.
Incubation period:	14–28 days.
Symptoms:	Diarrhoea/bloody diarrhoea.
Treatment:	Is usually supportive, plus metronidazole or tinidazole, then diloxanide furoate or paromomycin to eliminate cyst carriage.
Public health issues:	Note that cysts resist standard chlorination, but are destroyed by hyperchlorination.
	Household contacts should be screened microbiologically to detect carriage and cyst excretion (diloxanide furoate is also given to asymptomatic cyst carriers).
	Cases, apart from those in risk groups C and D (below) should be excluded from normal activities for 48 hours after first normal stool.
	Transmission is usually by F/O spread from a person who is chronically ill, or is an asymptomatic cyst carrier. Cases in risk groups C and D require one stool, negative for cysts, at least 1 week after end of treatment. Careful assessment of excreters is needed to evaluate significance because the cysts of *Entamoeba histolytica* are indistinguishable for those of the nonpathogenic *Entamoeba dispar*; referral to the reference laboratory may be required.

Campylobacter

Source:	FOOD; water.
Incubation period:	Usual 2–5 days, range 1–10 days.
Symptoms:	Fever, cramping abdominal pain, diarrhoea, bloody diarrhoea.
Treatment:	This is usually supportive with oral rehydration. For protracted illness, clarithromycin 500 mg q12h may be given for 5 days.
Public health issues:	Cases should be excluded from normal activities for 48 hours after first normal stool. Microbiological clearance is not required.
	Contacts of the patient can be monitored by clinical surveillance, bearing in mind that person-to-person transmission is uncommon, unless hygiene is poor and/or the case is faecally incontinent.
	Most outbreaks are due to cross-contamination of food, particularly when uncooked food, consumed raw, is prepared along with raw poultry. Transmission from infected food handlers is rare. Microbiological clearance of cases is not required.

CHAPTER 7 – *continued*

Cholera (*Vibrio cholerae*)

Source:	CONTAMINATED WATER; shellfish; raw food; washed food, F/O.
Incubation period:	Usual 2–3 days, range 4 hours–5 days.
Symptoms:	Profuse watery diarrhoea, with rapid dehydration.
Treatment:	This is supportive, with oral (or intravenous fluids). Patients would usually be admitted to an infectious diseases unit.
Public health issues:	Cases should be excluded from normal activities for 48 hours after first normal stool. Microbiological clearance is not normally required, but when indicated, two consecutive negative stool samples taken at least 24 hours apart are collected. Contacts who shared food and drink with the patient should have clinical surveillance for 5 days following the same exposure. Cholera is rare in the UK and is usually associated with imported cases. For person-to-person transmission to occur, a large inoculum is required.

Non-cholera vibrios (*Vibrio parahaemolyticus*)

Source:	FOOD (undercooked/contaminated shellfish).
Incubation period:	4–30 hours.
Symptoms:	Abdominal pain, diarrhoea.
Treatment:	This is symptomatic, with fluid replacement.
Public health issues:	Cases should be excluded from normal activities for 48 hours after first normal stool. Individuals with the same food exposure as the patient can be monitored by clinical surveillance for 48 hours after food was consumed. Infection is usually associated with travels returning from warmer climates. Although person-to-person spread has not been documented, as a precaution cases should be excluded from normal activities for 48 hours after first normal stool.

Cryptosporidium

Source:	F/O, utility company water, private water, farm animals, swimming pools.
Incubation period:	Usual 1–14 days.
Symptoms:	Watery/mucoid diarrhoea.
Treatment:	This is usually supportive, but seek advice for immunocompromised individuals.
Public health issues:	Cases should be excluded from normal activities for 48 hours after first normal stool. While microbiological clearance is not required, cases should also refrain from using swimming pools and recreational water features for at least 2 weeks after the first formed stool. Contacts of the patient should be monitored by clinical surveillance. Large numbers of oocysts, which are resistant to standard chlorination, are excreted in the acute infection. Person-to-person spread in the household, recreational, nursery, and health-care setting occurs. Immunocompromised individuals should drink boiled, cooled water if there is any risk of contamination.

Giardiasis (*Giardia lamblia*)

Source:	F/O (children), water, carrier to food.
Incubation period:	Usual 7–10 days, range 3–25 days.
Symptoms:	Diarrhoea and abdominal pain.
Treatment:	This is supportive, with metronidazole or tinidazole.
Public health issues:	Cases should be excluded from normal activities for 48 hours after first normal stool. Microbiological clearance is not required. As spread within households is common, contacts of the patient in this setting can be microbiologically screened to detect excreters, who will need treatment. Outbreaks linked to food and infected food handlers occur. Drinking water and recreational sports in rivers during foreign travel is relevant.

***Escherichia coli* O157 (VTEC)**

Source:	FOOD; farm animals; F/O, water.
Incubation period:	Usual 3–4 days, range 1–8 days.
Symptoms:	Cramping abdominal pain, diarrhoea, bloody diarrhoea, HUS, ARF. Hospital admission is required when there is bloody diarrhoea, to exclude HUS and ARF, and provide the appropriate support.
Treatment:	This is usually supportive, with oral rehydration. Antibiotics should not be used as they may increase release of the vero-toxin.
Public health issues:	Cases NOT in risk groups A–D should be excluded from normal activities for 48 hours after first normal stool. Cases and contacts in groups A–D should be excluded until clearance is obtained. Contacts in risk groups A–D should be screened, initially to identify excreters, and then to show microbiological clearance in any excreters identified. For microbiological clearance, two negative faecal specimens taken at an interval of at least 48 hours are required.

Norovirus

Source:	F/O, environment, vomit, food.
Incubation period:	Usual 24–48 hours, range 10–50 hours.
Symptoms:	Vomiting (with diarrhoea).
Treatment:	This is supportive.
Public health issues:	Cases should be excluded from normal activities for 48 hours after first normal stool. Microbiological clearance is not required. Contacts of the patient should be monitored by clinical surveillance for at least 48 hours after exposure to vomit, 'aerosolized vomit', and faeces. This is particularly important if the contact is employed in the health-care setting. Patients should not be transferred from, or admitted to, a health-care service without discussion with the receiving unit; the ambulance service should also be informed. Person-to-person spread is very common, and particular attention must be paid to environmental contamination with vomit, especially in eating and toilet areas. Food, especially ready-to-eat items exposed to vomit should be discarded, and food preparation areas rigorously cleaned. Particular attention has to be paid to cleaning soft furnishings, including carpets. Public health MUST be informed if there is any association with an institution, e.g. nursing home, school, university.

CHAPTER 7 – *continued*

Rotavirus

Source:	F/O.
Incubation period:	24–72 hours.
Symptoms:	Diarrhoea and vomiting. This can be severe for infants and children between 6 months and 2 years.
Treatment:	This is supportive, based on ORS. If this cannot be maintained due to severe vomiting, dehydration, and/or decreased consciousness, hospitalization must be considered for IV fluids.
	Public health issues: Cases should be excluded from normal activities for 48 hours after first normal stool. Microbiological clearance is not required.
	Contacts of the patient should be monitored by clinical surveillance.
	Adequate hygiene and toilet facilities should be provided. Carers should have stringent hygiene practices to prevent themselves acquiring the infection. In temperate climates, there is a characteristic activity peak in the cooler months of the year.

Salmonella (excluding typhoid and paratyphoid)

Source:	FOOD, exotic pets.
Incubation period:	Usual 12–36 hours, range 6–72 hours.
Symptoms:	Diarrhoea, vomiting, fever.
Treatment:	This is usually supportive, with oral rehydration. For protracted diarrhoea, ciprofloxacin (adults) 500 mg q12h may be given for 5 days; the antibiotic susceptibility profile must be checked first. Note caution for CDAD.
Public health issues:	Cases should be excluded from normal activities for 48 hours after first normal stool.
	No microbiological clearance is required in England and Wales, but in Scotland and the USA, individuals in certain risk groups require microbiological clearance.
	Contacts of the patient can be monitored by clinical surveillance.

Salmonella typhi/paratyphi

Source:	FOOD, carriers/excreters to food.
Incubation period:	Usual 8–14 days, range 3–30 days.
Symptoms: Enteric fever:	fever, headache, cough, abdominal pain.
Treatment:	Where enteric fever is a consideration, consider prompt referral to A & E for review and collection of blood cultures. The patient must be admitted to a side room. When the organism is identified in blood culture confirming enteric fever, treatment is for 14 days with the appropriate antibiotic, e.g. amoxicillin, depending on the antibiotic susceptibility profile.
Public health issues:	Stool specimens should be collected from all household contacts, and others assessed to have a similar exposure to the index case in the month prior to the onset of illness in the index case. Chronic urinary carriage can occur, but is rare.
	Faecal contamination of food by carriers occurs. Patients (plus contacts, excreters, and carriers) in risk groups A–D are excluded until microbiological clearance; specific protocols exist for other individuals. This is the domain of the public health department.

Shigella

Source:	F/O.
Incubation period:	Usual 1–3 days, range 12 hours–7 days.
Symptoms:	Fever, cramping abdominal pain, diarrhoea, bloody diarrhoea.
Treatment:	Infections are usually mild with *Shigella sonnei*. Treatment is thus usually supportive, with oral rehydration. For the other shigellae, antibiotics are frequently used.
Public health issues:	Cases with *Shigella sonnei* should be excluded from normal activities for 48 hours after first normal stool. Cases in risk groups A–D with *Shigella dysenteriae*, *Shigella flexneri*, and *Shigella boydii* require microbiological clearance. Contacts in risk groups A–D of cases with *Shigella dysenteriae*, *Shigella flexneri*, and *Shigella boydii* should be screened microbiologically, otherwise only clinical surveillance is required. For microbiological clearance, two negative faecal specimens taken at an interval of not less than 48 hours is required. Person-to-person spread is common. In the nursery setting in particular, hand washing and toilet facilities must be assessed for adequate hygiene.

Yersiniosis (*Yersinia enterocolitica*)

Source:	FOOD, pigs, F/O.
Incubation period:	3–7 days.
Symptoms:	Fever, abdominal pain (may mimic appendicitis in children; mesenteric adenitis), diarrhoea.
Treatment:	As enterocolitis and mesenteric adenitis are self-limiting, supportive treatment is usually appropriate. Advice should be sought when symptoms persist. (Serology tests are available for the retrospective diagnosis of yersiniosis.)
Public health issues:	Cases should be excluded from normal activities for 48 hours after first normal stool. Microbiological clearance is not required. Individuals with the same food exposure as the patient can be monitored by clinical surveillance for 24 hours after food was consumed. The reservoir is the gastrointestinal tract of animals and birds, and water. The organism reproduces at 4°C. Contaminated food, and pork in particular, are relevant.

CHAPTER 9

Details of the organisms listed in **148**, and the role that serological tests have in screening, determining immunity, assessing the risk after exposure of a nonimmune individual, and in confirming infection. (The organisms are listed alphabetically here.) The list of Notifiable Diseases, Chapter 1, **8** (UK) and **9** (USA) should be referred to; prompt notification and involvement of the public health department in the management of the named conditions is essential. The information given here is a summary, and is generally relevant to adult patients. For HAV, HBV, HCV, and HEV, numbers refer to the relevant figures in Chapter 9.

CMV		Transmitted by intimate mucosal contact (kissing, sexual intercourse), and blood transfusion. The incubation period is 3–8 weeks. There is prolonged virus shedding for many months after the primary infection. The infection is often asymptomatic, but in the 25–35 year age group, the acute infection is an infectious mononucleosis (IM)-type syndrome (see EBV). CMV differs from EBV in the low incidence of pharyngitis and lymphadenopathy, but the diagnosis should be considered in a young adult with fever and hepatitis, with a blood film showing atypical lymphocytes. Note that acute CMV infection in pregnancy can result in congenital malformation.
Infection	✔	Acute infection: Test for specific IgM antibodies. Blood film can show atypical lymphocytes. Serum test for heterophile antibodies (Monospot) are usually negative in CMV infection. CMV PCR (EDTA blood) is used to diagnose active infection, and to monitor viral load in immunocompromised patients, including renal transplant patients, oncology, and haematological malignancy patients under the care of the specialist team. CMV colitis can occur in other immunocompromised patients, for example those under the care of the rheumatologists. Chronic diarrhoea (>14 days) in these patients should prompt the consideration of CMV colitis, and a PCR test done.
Immune status	✘	IgG antibodies are a marker of past infection only, and do not relate to immunity.
Screen	✘	Not usually done, but screening for IgG antibodies is important in the assessment of donors and recipients individuals who are to undergo transplantation.

EBV

Transmitted by intimate oral contact, such as prolonged kissing.

The incubation period is estimated to be 30–50 days.

While defining EBV infection, the unifying feature of IM syndrome is an atypical lymphocytosis, which can be seen with CMV, toxoplasmosis, viral hepatitis, acute HIV infection, rubella, lymphoma, and leukaemia.

Clinical features of EBV include sore throat, fever, sweating, anorexia, marked headache, and malaise. Swollen red tonsils and general lymphadenopathy, particularly cervical, splenomegaly, enlarged liver, and jaundice occur.

The infection usually resolves in days, but it may last for several weeks, followed by profound lethargy. Heterophile (Monospot) antibodies, which are not directed against the virus, are present in up to 85% of cases, with an atypical lymphocytosis of up to 15×10^9/L confirming the diagnosis. Heterophile antibody is more likely to be absent in paediatric population.

Infection ✔

Acute infection: Blood film for atypical lymphocytes, and serum test for heterophile antibodies (Monospot). If these are negative, commonly in children, EBV serology should be requested. IgM to virus capsid antigen (VCA) is consistent with acute infection. Alternatively IgG antibodies to VCA and EBNA (EB nuclear antigen) can also be used to approximate the stage of the infection. Individuals who are VCA IgG antibody positive but EBNA IgG antibody negative are likely to be in the early stage of infection, whereas those who are both VCA IgG and EBNA IgG positive indicates >3 months since acute infection. This is because unlike VCA IgG, EBNA IgG antibodies appear late (>3 months) after the acute infection.

	Acute infection	Previous infection (>3 months)
IgM to VCA	+	+/–
VCA IgG	+/–	+
EBNA IgG	–	+

EBV PCR (EDTA blood) is used to diagnose active infection, and monitor viral load in immunocompromised individuals such as renal transplant patients.

Immune status ✘

IgG antibodies are a marker of past infection only, and do not relate to immunity status.

Screen ✘

Not usually done, but screening for IgG antibodies is important in the assessment of individuals who are to undergo transplantation.

HAV (157)

Transmitted by the faecal–oral route (including food, water) and by sex (anal–oral).

The incubation period is about 45 days (range 20–60). Infectivity is maximum during the latter half of the incubation period to a few days after the appearance of jaundice.

The infection is usually asymptomatic, especially in children. Symptoms include fever, nausea, anorexia, right upper quadrant (RUQ) discomfort, and the usual features of jaundice.

Infection ✔

Acute infection: Test serum for IgM antibodies. These can persist for several months after onset of the acute infection. IgM antibodies present = acute/recent infection. IgM antibodies absent = no evidence of acute/recent infection.

Immune status ✔

Testing for immunity is not usually recommended, but patient may request confirmation of IgG status following vaccination. The laboratory report can read: 'IgG antibodies DETECTED; evidence of past infection or immunization'.

Vaccination is recommended for those travelling to or going to reside in high or intermediate prevalence areas, patients with chronic liver disease, haemophiliacs, MSM with multiple sexual partners, IDU, or where there is an occupational risk (laboratory workers who may be exposed to the virus, staff at large residential institutions, or day-care facilities), sewage workers, people who work with primates, selected groups of food handlers. The local public health department, and the 'Green Book'[14], and www.nathnac.org can be referred to.

Screen ✘

Population-based screening is not usually done.

CHAPTER 9 – *continued*

HBV (158–162)		Blood borne by mucosal contact (sexual and perinatal), skin penetration (for example 'sharps' injuries, tattoo and acupuncture clinics). Semen, vaginal fluid, and saliva should be considered infectious. The incubation period is 60–90 days (range 45–180). Where there is a sexual history, the patient should be referred to the STD clinic for a full STD screen. The acute infection is usually asymptomatic, especially in children, and up to two-thirds of adults. Insidious onset of RUQ discomfort, jaundice, arthralgia, rash, occur in symptomatic individuals. The important issue with HBV is chronic infection, and rates are at least 70% in children exposed perinatally or in early childhood, falling to <10% in adults after acute infection.
Infection	✔	Acute infection: Test for HBcIgM (and HBsAg); the presence of these markers confirms acute infection. Chronic infection: Test for HBsAg, and if positive for HBcIgG and the 'e' markers. Chronic carriage is confirmed if HBsAg, HbcIgG, HbeAg/HBeAb positive, and HBcIgM is negative. HBV PCR (EDTA blood) is used to determine viral load and monitor the effectiveness of treatment.

Immune status	✔	The patient has received full course of vaccination; test for HBsAb 6–8 weeks after last dose. HBsAb titres:
		• 100 mIU/mL = immune. Give a booster dose at 5 years. There is no need to retest antibody levels either before or after the booster in immunocompetent individuals.[14]
		• 10–100 mIU/mL = immune but give further booster dose of vaccine, and the 5 year follow-up dose. There is no need to retest antibody levels either before or after the booster in immunocompetent individuals.[14]
		• <10 mIU/mL (and the same result is obtained after a further course of vaccine).
		  • The individual is a true nonresponder to the vaccine (if they have completed two full courses of vaccine), and is susceptible to infection. Those at occupational risk should be advised to contact their occupational health departments.
		  • The individual is a chronic carrier. He/she should be counselled and have serum tested for HBcAb and HBsAg to determine if this is the case. If the patient is from a part of the world where there is a high prevalence of chronic HCV infection, counselling and testing should be considered promptly.
		  • If the individual is obese, it is possible that the vaccine has not been delivered into the deltoid muscle; a full course of vaccine should be considered with an appropriate length needle.[6, 7]
		Vaccination is recommended for close family contacts of an individual with acute or chronic infection, foster carers, families adopting children from high or intermediate prevalence area (in due course these children should be screened to determine their HBV status, in view of the benefits of treatment), those travelling to or going to reside in high or intermediate prevalence areas, patients with chronic liver disease, chronic renal disease, individuals receiving regular blood products and their carers, staff and inmates in custodial institutions, individual who change sexual partners frequently, IDU, or where there is an occupational risk (all HCW and students working in health care, staff at residential institutions for learning difficulties, morticians and embalmers). The local public health department, the 'Green Book'[14] and www.nathnac.org can be referred to.

Screen	✔	Population-based screening involves testing all pregnant women at the first antenatal visit for HBsAg. Patients who are HbsAg positive are tested for HBcIgM (to exclude acute infection), HBcIgG, HBeAg, and HBeAb. The newborns of 'low-risk' mothers (eAg-/eAb+) are started on a rapid course of HBV vaccine at birth. Newborns of 'high-risk' mothers (HBeAg+/HBeAb-) are also given HBIG at birth. Acute HBV in pregnancy would be regarded as 'high risk'. Individuals from areas of the world with high prevalence should be screened for chronic carriage.

HCV (163)		Transmitted by blood (contaminated blood-products, 'sharps' injuries, IDU). Transmission associated with household contacts and by sex is considered a low risk. The incubation period is 60-90 days (range 45-180). Most infections are asymptomatic, but any patient with nausea, anorexia, RUQ discomfort and/or jaundice, particularly in 'risk' groups, should be tested.
Infection	✔	Acute infection: Seldom diagnosed as patients are not usually symptomatic. This would however be investigated in an individual who had had a 'sharps' injury from a known infected individual. Testing for HCV RNA by PCR and HCV antibody at 4–6 weeks after the injury, followed by these tests at 3 and 6 months.[13] These cases must be managed by the STD physicians, medical virologist, and the appropriate occupational health department. Chronic infection: The laboratory tests for HCV antibodies and if they are present the laboratory must test plasma/serum for HCV RNA by PCR. • HCV antibodies and RNA detected = CHRONIC HCV infection. • HCV antibodies detected; RNA NOT detected = evidence of past infection only. (A repeat specimen should be tested to confirm the negative RNA status of such an individual.) These individuals are NOT immune to reinfection, as the antibody response is heterogeneous, and there are six HCV genotypes. HCV PCR (EDTA blood) is used to determine viral load, genotype, and monitor the effectiveness of treatment.
Immune status	✘	Antibodies produced in HCV infection are heterogeneous, and are thus NOT protective.
Screen	✔	Population-based screening may be considered appropriate for high-risk groups, e.g. IDU.

CHAPTER 9 – *continued*

Helicobacter

Helicobacter pylori is usually acquired in childhood, and its prevalence in older age groups is thought to reflect a cohort effect related to poorer living conditions of children in their previous decades of life.[15] At least 50% of the world's population is infected.[16] Helicobacter infection is a cofactor in development of duodenal and gastric ulcers, gastric cancer, and gastric mucosa-associated lymphoid-tissue (MALT) lymphoma, occurring in 1–10%, 0.1–3% and <0.001% of infected individuals respectively.[17] The diagnosis and treatment of helicobacter infection does benefit patients with ulcer disease, about 8% of patients with functional dyspepsia, and it reduces future risk of ulcer disease, gastric cancer, and the risks associated with long-term proton-pump inhibitors (PPIs).[18]

(Note that 'alarm symptoms' for upper gastrointestinal tract [GIT] neoplasia are dysphagia, persistent vomiting, upper GIT bleeding, and weight loss.[18] In addition, it is important to note that all patients over 54 years of age, who present with unexplained, persistent dyspepsia, of over 4–6 weeks duration should be referred for urgent endoscopy.)[20]

There are some differences in the testing and treatment recommendations of various guidelines of the American College of Gastroenterologists,[19] NICE,[20] the Maastricht III consensus,[21] and the HPA Guidance.[22]

In general testing for *Helicobacter pylori* is recommended in the following groups of patients:

- Those with a past history of gastric ulcer or duodenal ulcer who have not previously been tested for helicobacter.
- Those with uncomplicated dyspepsia (no 'alarm symptoms'; see above) that is not responsive to lifestyle change (alcohol/smoking), antacids, H_2 antagonists, or one month of a PPI.
- Those with chronic nonsteroidal anti-inflammatory drug (NSAID) use, without ulcer history, where eradication of helicobacter will reduce the risk of peptic ulcers and/or bleeding, but will not remove all the risk.
- Routine testing is not recommended in patients with gastro-oesophageal reflux disease.[22]

Tests

- The breath test has a specificity and sensitivity of 95%, and relies on the ability of the powerful urease enzyme of helicobacter to convert ^{13}C-urea, in an oral solution, to ammonia and $^{13}CO_2$, with the gas in expelled breath then being measured. The patient swallows the capsule, and their breath is collected at 0 and 20 minutes for assay. This test is available on prescription; local arrangements for testing, for example with the gastroenterology department should be available. There is a kit available for children, but the appropriateness of testing in this age group has not been established.[23]
- The stool antigen test for helicobacter has a sensitivity and specificity of 97%, and is the test of choice. A nutmeg-sized sample of stool should be submitted. The request form must be clearly labelled for this test; formed stool would usually be discarded by the laboratory!
- With the urea breath test and stool antigen test, the patient must not have taken PPI for at least two weeks, and antibiotics for at least 4 weeks (and at least 24 hours for those taking H_2 antagonists), before testing. There may be suppression of growth of the organism and a false-negative result could be obtained.
- Blood tests to detect the presence of antibodies to helicobacter have a sensitivity and specificity of 85–92%. They should not be used in the older adult (>54 years), children, and post treatment. The presence of antibody means either:
  - The patient was infected at the time of the test.
  - There has been past infection which has resolved spontaneously, or it has been treated.
  - The test may be detecting nonspecific antibodies.

Treatment

Treatment should be based on a positive result, preferably based on a breath test or stool antigen test.

Patients with a negative test should be considered as having functional dyspepsia, and treated with a low-dose PPI or H_2 antagonist for 1 month as required.[21]

Treatment options are given in Chapter 11. It is generally recommended that clarithromycin or metronidazole should not be used if they have been used in the past year for any infection.[22]

For patients who are positive, an 85% eradication rate is achieved with compliance to the eradication regime. Patients who are asymptomatic after treatment should be reassured that treatment has been effective; there is usually no need to check for clearance.[22]

(*Continued*)

Helicobacter *continued*

When to retest

When retesting, the breath test should be used, with the faecal antigen test as an alternative; serology should not be used. Retesting must not be done within 4 weeks of completion of treatment to avoid false-negative results. Eradication can also be confirmed by testing during repeat endoscopy for patients in whom repeat endoscopy is required.

Confirmation of eradication of helicobacter should be done in the following patients:

- Patients who have had a *Helicobacter pylori*-associated ulcer or gastric MALT lymphoma.[19–22]
- Patients who have undergone resection for early gastric ulcer.[19, 21]
- Follow-up testing can be indicated in patients whose symptoms of dyspepsia are recurrent or persist after eradication treatment. This will avoid repeat treatment of patients whose symptoms are in fact not attributable to *Helicobacter pylori*.[15] This should be balanced with consideration of such patients who are likely to have functional dyspepsia, where a low-dose PPI or H_2 antagonist can be considered for 1 month and then as required.[22]

Immune status: Not relevant

Screening: The European guidelines recommend diagnosis and then eradication of helicobacter infection in first-degree relatives of patients with gastric cancer and in patients with gastric atrophy, unexplained iron-deficiency anaemia or chronic idiopathic thrombocytopenic purpura, although the data to support these recommendations are currently limited.[21]

HEV (164)

Transmitted by faecal–oral route, including food and water. Often travel associated but should still be considered in cases of infectious hepatitis without a travel history, when the more common agents have ben excluded. The incubation period is about 45 days (range 20–60), with stool shedding of virus for 2 weeks before and after symptoms appear.

The infection is usually asymptomatic, especially in children. Symptoms include fever, nausea, anorexia, RUQ discomfort, and the usual features of jaundice. Severe infection can occur in pregnancy, with up to 20% mortality recorded in the third trimester; pregnant individuals should be advised not to travel to endemic areas.

Infection	✔	Acute infection: test serum for IgM antibodies. IgM antibodies detected = acute infection (NOTIFY PUBLIC HEALTH). IgM antibodies not detected = no evidence of acute infection.
Immune status	✘	Because there are five genotypes of the virus, the roles of IgG antibodies in long-term immunity are unclear.
Screen	✘	Not done.

CHAPTER 9 – *continued*

HIV		Blood borne (congenital, perinatal, sex, IDU), and secretions, e.g. genital tract, breast milk, etc. Primary HIV infection occurs after an incubation period of 2–4 weeks (range 1–12 weeks) and usually starts abruptly, and lasts for 2–14 days, mimicking IM, with fever, sweats, lethargy, malaise, sore throat, headache, photophobia, arthralgia, myalgia, and diarrhoea. A truncal maculopapular rash, cervical and axillary lymphadenopathy, meningoencephalitis, and peripheral neuropathy can also occur. Opportunistic infections, such as candida oesphagitis and pneumocystis pneumonia, occur. A HIV test should be considered in anyone presenting with an IM-like illness especially if they are in a high-risk group. HIV infection is usually asymptomatic and chronic for years until the development of AIDS. Presenting conditions such as pulmonary TB, particularly in high-risk individuals, should prompt the consideration of HIV.
Infection	✔	Acute and chronic infection: The combination test for p24 antigen and HIV antibody can detect the infection from about 3 weeks after exposure. The first test can be done 4 weeks after a possible exposure.[13] HIV PCR may be considered in certain situations in the acute infection stage, based on the advice of the medical virologist. The PCR is used to determine viral load, and monitor the response to treatment.
Immune status	✘	No natural immunity via protective antibody exists for this chronic infection of T4, and other cells of the cell-mediated immune system.
Screen	✔	Population-based screening involves testing all women at the first antenatal visit for HIV antibody and antigen tests. It is reasonable to consider retesting later in pregnancy to women in 'high-risk' population groups. In addition, the test should be offered to any individual attending the practice/clinic who may consider themselves to have had a potential exposure. Note that current serology tests for antigen/antibody do not detect the virus for at least 3 weeks after exposure. A repeat test should always be done 3 months after the last exposure.

Leptospirosis		Contact of mucous membranes or abraded skin with water, moist soil, vegetation, fomites, contaminated with the urine of domestic and farm animals and rodents is the usual source. The incubation period is 5–14 days, median 10 days. (In adults visiting areas where there may be a high risk of acquiring the infection, for example rivers in tropical areas of southeast Asia, doxycycline 200 mg once a week may be considered for the duration; amoxicillin is not likely to be as effective.) The infection is often abrupt in onset, with high fever, headache, chills, rigors, myalgia, and conjunctival suffusion.
Infection	✔	Acute infection: IgM appear from about the fifth day of illness (note incubation period above) with the disappearance of leptospira from the blood; IgG antibodies then appear. The antibody response may be delayed or suppressed if there is current antibiotic treatment. Acute infection: IgM antibody DETECTED.
Immune status	✘	Immunity is not a consideration in this infection.
Screen	✘	Not done.

Lyme disease		*Borrelia burgdorferi* is transmitted by hard-bodied ticks. There is a delay of at least 24 hours between tick attachment and transmission. While adult ticks are more infectious than nymphs, they are more likely to be seen and removed before transmission. Transmission is more likely to occur when the nymphs, which can be difficult to see, take their first blood meal. This often occurs in late spring, early summer and autumn. It is useful to have knowledge of endemic areas in individual countries (see Chapter 1, **22**). Erythema migrans (EM) is the classic presentation, appearing 3–30 days after tick exposure (constitutional symptoms are usually minor in early EM). A full body examination should be done, as EM can occur in unusual places for cellulitis, such as the axilla, back, and popliteal fossa, and should be carefully looked for in the setting of malaise, fatigue, headache, lymphadenopathy, and arthralgia, often of the knee. All the details, including dates of tick exposure, symptoms and signs, and antibiotic use must be recorded on the request form.
Infection	✔	The Lyme Borreliosis Unit of the HPA makes the following comments concerning the serological diagnosis of Lyme disease.[24] These are: • Antibody tests should not be requested 'routinely' if the clinical findings and tick exposure risk assessment do not give evidence for Lyme borreliosis. • Antibody tests may be negative for several weeks after the individual has been infected, due to the low level of antigenic stimulation in the early stages of infection. • Laboratory tests are not routinely recommended for confirming the clinical diagnosis of EM. • The majority of patients who have symptoms of early disseminated infection (e.g. facial palsy or meningitis) are seropositive at presentation, and those who are seronegative usually seroconvert within 2–3 weeks. • Laboratory tests are recommended to support the diagnosis of disseminated Lyme borreliosis, as none of the later manifestations of the disease are unique to this infection. These include facial palsy, radiculopathy, arthritis usually affecting the knee, encephalomyelitis, and lymphocytic meningitis. • Antibody tests are rarely negative in late Lyme borreliosis, which includes Lyme arthritis and late encephalomyelitis. • Antibody positivity may be related to past rather than current infection, emphasizing the importance of careful assessment of the tick exposure and clinical findings. • It is uncommon for the signs and symptoms of disseminated Lyme borreliosis to present later than 1 year after infection, although recognition may be delayed due to lack of awareness of the condition.
Immune status	✘	Immunity is not a consideration in this infection.
Screen	✘	Not done
Prevention		Prevention measures should always be taken in endemic areas: Wear: Light-coloured clothing, with long trousers tucked into socks and long-sleeved shirts. Use: Repellents, e.g. DEET. Avoid: Contact with brush/bush. Stay: On paths. Search: Exposed skin every 3–4 hours when outside. Check: All skin areas, especially axillae, groins, and thighs, and the head and neck of children when inside.

CHAPTER 9 – *continued*

Measles		Respiratory-borne. The incubation period is about 10 days to the prodromal period, with the rash appearing about 2–4 days later.[26] Individual should be considered infectious from the beginning of the prodromal period to 4 days after the appearance of the rash. Strongly suggestive of measles is a prodromal period with a erythematous and maculopapular rash (at least 3 days), fever (at least 1 day), coryza, cough, and conjunctivitis. Koplik's spots (small red spots with blueish-white centres) may appear on the mucous membrane of the mouth 1–2 days before, and 1–2 days after the appearance of the rash. Notify public health.
Infection	✔	Acute infection: Serum tests for IgM (and IgG) antibodies are available via the medical microbiology department. A throat swab cut into VTM, or urine in plain white-topped sterile container can also be submitted for measles PCR (**149–153**). Acute infection: IgM antibody: DETECTED or measles virus detected by PCR. Notify public health.
Immune status	✔	Measles IgG antibody test can be done. Exposed individuals who are immunocompromised or pregnant or HCW where there is no good history of immunization are examples of where immunity testing may be warranted. Note that HCW with documented evidence of IgG antibodies to measles, or two doses of MMR vaccine are considered immune.[14] The objective of vaccination programs is to give two doses of MMR vaccine at appropriate intervals to all eligible individuals. About 90% of individual will seroconvert to measles, mumps, and rubella after the first dose of vaccine.[25] Vaccination includes all those with an unknown or incomplete vaccination history, HCW who do not have satisfactory evidence of immunity (two doses of MMR, or positive antibody tests for measles and rubella). Individuals travelling or going to reside abroad in an endemic or epidemic region should be fully immunized according to national schedules; specific advice should be followed for children in these circumstances.[26]
Screen	✘	Population-based screening is not usually done, but see HCW above.

Mumps		Respiratory-borne. Incubation period to the prodromal period, of fever, headache, malaise, myalgia, anorexia is about 14 days, followed several days late by the appearance of bilateral, occasionally unilateral parotid swelling. The individual is infectious from the beginning of the prodromal period and up to 10 days after the appearance of parotitis. Exposed individuals should be considered infectious from 12–15 days after exposure. Signs include bilateral, occasionally unilateral parotid swelling. Pancreatitis 5%, oophoritis 5%, or orchitis 25% (both post pubertal) may be the only sign. Asymptomatic infection is common in young children. Notify public health.
Infection	✔	Acute infection: Detection of mumps IgM in saliva collected 1–4 weeks after onset of illness can be done. Serum tests for IgM (and IgG) antibodies are available via the medical microbiology department. A throat swab cut into VTM, or urine in plain white-topped sterile container can also be submitted for measles PCR (**149–153**). Acute infection: IgM antibody DETECTED, or mumps virus detected by PCR.
Immune status	✔	Mumps IgG antibody test can be done. (Note that for HCW with documented evidence of IgG antibodies to measles and rubella, or two doses of MMR vaccine are considered immune.[14] (The objective of vaccination programmes is to give two doses of MMR vaccine at appropriate intervals to all eligible individuals. About 90% of individual will seroconvert to measles, mumps, and rubella after the first dose of vaccine.[25] Vaccination includes all those with an unknown or incomplete vaccination history, HCW who do not have satisfactory evidence of immunity (two doses of MMR, or positive antibody tests for measles and rubella). Individuals travelling or going to reside abroad in an endemic or epidemic region should be fully immunized according to national schedules; specific advice should be followed for children in these circumstances.[26]
Screen	✘	Population-based screening is not usually done, but see HCW above.

Parvovirus B19		Respiratory-borne. The incubation period to the appearance of the rash is about 15 days. The individual is infectious from about 8 days before the rash appears. The classic rash is 'slapped cheeks' in children. Parvovirus should be considered in the differential diagnosis of anyone with a maculopapular rash who is either pregnant, or works in health care. Parvovirus infection can be difficult to distinguish from acute rubella infection, both also capable of producing an arthralgia. Rubella cannot be distinguished from parvovirus B19 clinically. Parvovirus affects rapidly dividing cells such as the marrow and as a result subclinical anaemia occurs. However, in individuals with haemopoietic disorders where there is little bone marrow reserve, acute parvovirus infection can render them temporarily aplastic.
Infection	✔	Acute infection (see Chapter 10): Request test for IgM (and IgG) antibodies. In the patient who is IgM positive and is less than 20 weeks pregnant, there is a risk that the foetus will be infected, with resulting abortion or hydrops foetalis. The obstetrician and medical microbiologist/virologist would be involved. Infection later in pregnancy does not appear to be a risk. Parvovirus B19 PCR (EDTA blood) is available for diagnosis of active infection in selected patients, e.g. the immunocompromised patient.
Immune status	✔	A pregnant woman promptly reporting contact with a suspected case of parvovirus B19 should have IgM and IgG antibodies tested. If the patient is IgG antibody positive, she is considered immune; if she is negative for IgG and IgM antibodies, serology should be repeated 4 weeks later.
Screen	✘	Population-based screening is not usually done. In outbreak years, there may be concern among particular groups such as female schoolteachers of child-bearing age.

Rubella		Respiratory-borne. The incubation period to the appearance of the rash is 14–21 days. The individual is infectious 7 days before and 4 days after the appearance of the rash. Lymphadenopathy involving post-auricular and suboccipital glands may precede the rash by 24 hours. The rash is usually transitory, erythematous and mostly seen behind the ears and on the face and neck. Clinical diagnosis is unreliable, as the rash is not specific. The rashes of rubella and parvovirus are indistinguishable clinically.
Infection	✔	Acute infection: Rubella IgM antibodies DETECTED. Notify public health.
Immune satus	✔	Rubella IgG antibody test can be done. (Note that for HCW those with documented evidence of IgG antibodies to rubella, or two doses of MMR vaccine are considered immune). The objective of vaccination programmes is to give two doses of MMR vaccine at appropriate intervals to all eligible individuals. About 90% of individual will seroconvert to measles, mumps, and rubella after the first dose of vaccine.[25] Vaccination includes all those with an unknown or incomplete vaccination history, HCW who do not have satisfactory evidence of immunity (two doses of MMR, or positive antibody tests for measles and rubella). Individuals travelling or going to reside abroad in an endemic or epidemic region should be fully immunized according to national schedules; specific advice should be followed for children in these circumstances.[26] A pregnant woman reporting contact with a confirmed or suspected case of rubella who is IgG antibody positive is immune. If she is negative for IgG and IgM antibodies, the IgM and IgG antibody test should be repeated 4 weeks later (see Chapter 10).
Screen	✔	Part of routine antenatal screening (see Chapter 10).

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Schistosomiasis		Water-borne parasitic infection. The production of eggs by the female parasite begins 4–6 weeks after exposure. Katayama syndrome, an immune response to the eggs, with chills, headache, myalgia, abdominal pain and diarrhoea occurs mainly with *Schistosoma mansoni* and *Schistosoma japonicum* infection. Terminal haematuria and dysuria may be the presenting symptoms of *Schistosoma haematobium* months or years after infection. Left untreated, scarring and distortion of the urinary tract together with carcinoma may result.
Infection	✔	Test for IgG antibodies. Antibodies appear from 6 weeks after exposure, and the individual should be tested about 12 weeks after the last exposure. A person who has history of travel or residence in an endemic area, with any positive serology result, should be treated with praziquantel (20 mg/kg followed 4–6 hours later by one further dose of 20 mg/kg). (See BNF for *Schistosoma japonicum* treatment). Infection with *Schistosoma haematobium* can be diagnosed by checking for ova in urine at 3 and 6 months after the last exposure (see below). A *terminal stream* (10–20 mL) of urine is collected into a white-topped container between noon and 3 p.m. after 10 minutes of light exercise, e.g. walking up and down stairs. (Gravity, exercise, and the contraction of the trigone at termination push eggs out of the bladder wall into the urine). If there are any doubts serology should be performed.
Immune status	✘	Not done. Antibodies are a marker of infection only and do not relate to immunity.
Screen	✘	(Not usually done, but should be considered in patients originating from parts of the world where this infection is endemic, for example sub-Saharan and east Africa, for example patients attending a refugee/asylum centre).

Toxoplasmosis		The incubation period is 1–3 weeks. Oocysts in cat faeces require at least 24 hours to sporulate and become infective. Toxoplasmosis can be acquired following direct contact with the excreta of cats and farm animals. Undercooked pork and lamb, as well as unpasteurized goat's milk are other sources. Uncooked eggs are another source. Exposure should be reduced by keeping cats away from kitchen working surfaces during food preparation in particular, cleaning litter boxes daily, with boiling water. The use of disposable gloves, and hand washing when cleaning cat litter and gardening are important in reducing exposure. Most cases of toxoplasmosis are asymptomatic, and less than 5% of cases present with an IM-type syndrome, consisting of fever, malaise, night sweats, maculopapular rash, and hepatosplenomegaly. Less than 10% of cases have significant lymphadenopathy. The differential diagnosis includes Hodgkin's and other lymphomas.
Infection	✔	Most infections are asymptomatic. The patient presenting with an IM-type syndrome, especially during pregnancy, should have blood collected for toxoplasmosis serology. (Total antibody tests are done in most routine laboratories, and positive samples are sent to the reference laboratory for confirmatory IgM and IgG tests to determine if the infection is acute or latent.)
Immune status	✘	Not done. Antibodies are a marker of infection and do not relate to immunity. Cell-mediated immune system suppresses the organism, which can be reactivated in immunosuppressed conditions, e.g. AIDS.
Screen	(✔)	Anetnatal screening is not done routinely in the UK, as congenital toxoplasmosis is uncommon. Routine screening prenatally and during pregnancy was introduced in a number of European countries when the seroprevalence of the disease is much higher. Individual patients may request screening.

Treponema		Sexually transmitted. The incubation period for primary syphilis is 2–10 weeks. Individuals are infectious in primary and secondary disease, and intermittently in latent syphilis. Syphilis is a chronic infection that has primary, secondary, and latent stages. Anyone with positive serology should be referred promptly to the STD clinic. Treponemal specific antibody tests once positive remain so for life.
Infection	✔	For acute, latent, or reactivated infection, VDRL/RPR, and treponemal IgM/IgG antibodies are tested. The patient with positive results must be referred to the STD clinic. (The child born to a treated mother who is IgG antibody positive will acquire antibodies passively by transfer across the placenta. In addition to clinical assessment to exclude congenital syphilis, and IgM/IgG antibody tests at birth, the child is then monitored for loss of the maternal passively acquired antibodies over a period of 12 months; Chapter 10, **174**.)
Immune status	✘	The infection is chronic and latent, and antibodies do not confer immunity.
Screen	✔	Screening is part of the first routine antenatal visit. Older patients with dementia and other neurological conditions are usually screened. A patient may request a screen following a possible exposure in the past. Serum is tested for treponemal IgG antibodies, and if these are positive, IgM and VDRL/RPR antibodies are done. IgM antibodies are markers of acute infection. VDRL/RPR antibody titres >1/8 are nonspecific markers of active infection. Anyone found to have treponemal antibodies should be referred to the STD clinic.

VZV		The incubation period from exposure to the appearance of the rash is about 10–21 days, with a prodromal period, of malaise and fever starting about 2 days before the appearance of the rash. Transmission is via the respiratory route (chickenpox), and direct contact with the noncrusted rash of chickenpox or exposed herpes zoster. (Note that immunocompromised individuals with herpes zoster are considered to be infectious irrespective of whether or not the rash is covered, as shedding of virus is much greater). Chickenpox has a prodromal period before the appearance of the maculopapular, then vesicular rash, which is usually itchy, and mainly on the face and trunk. After a period of 4–5 days the rash begins to crust. Secondary infection with group A streptococcus can be a serious complication. Chickenpox pneumonia is a serious but uncommon complication in adults. It is more frequent in smokers and pregnancy is thought to be an added risk. The fetus can be affected, see Chapter10. Herpes zoster is dermatomal reactivation of latent virus.
Infection	✔	The diagnosis is usually clinical. A swab of an opened lesions is cut into VTM, and tested for VZV by PCR. IgM antibody tests can be done, but PCR is the preferred option.
Immune status	✔	Test for IgG antibodies. IgG antibodies are protective; the individual who is IgG negative is susceptible (see Chapter 10). (HCW with a definite history of chickenpox, or who have been vaccinated, should be considered immune.)
Screen	✘	Population-based screening is not done, but is done for HCW

CHAPTER 9 – *continued*

Shingles	Shingles or herpes zoster infection arises due to activation of latent VZV, and is characterized by a unilateral eruption with a dermatomal distribution; the thoracic and lumbar regions are most commonly involved. Facial zoster can involve the eyelids, and the eye. Involvement of the eye can result in a life-threatening herpes ophthalmicus or keratitis; the ophthalmologist must be contacted promptly. The unilateral skin eruption is preceded by pain in the dermatomal area about 24–48 hours before the appearance of the erythematous, maculopapular lesions which evolve into the vesicular rash. The affected area can be intensely painful, with an associated paraesthesia. Herpes zoster in the immunocompromised can be more severe, with the risk of disseminated zoster.
Diagnosis	The diagnosis is usually clinical. If there is any doubt about the diagnosis, particularly in the immunocompromised, direct testing of lesions is essential; lesions can be carefully broken, a swab rubbed gently in the base. The swab is then shaken in VTM, and this specimen is processed in the laboratory by VZV PCR. (A dry swab can be used in the absence of VTM; **149–153**.) Individuals with herpes zoster will be IgG antibody positive; a pregnant woman with zoster can be reassured that these antibodies will protect the fetus. Individuals with zoster can be infectious for up to 7 days after the appearance of the rash. However, the risk of acquiring VZV infection, i.e. chickenpox, from an immunocompetent individual with nonexposed zoster lesions (thoracolumbar/trunk) is remote. There is a risk of acquiring VZV from an immunocompromised patient with herpes zoster on any part of the body, as viral shedding may be greater.[14]
Prevention	Because the morbidity associated with herpes zoster and post-zoster neuralgia in the older individual, antiviral treatment must be used at the earliest opportunity after lesions appear. It is now considered reasonable to consider vaccinating all immunocompetent individuals aged 60 and over with the live, attenuated VZV vaccine.[27] (Oka/Merck strain, Zostavax, Merck, Sharp & Dohme).

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CHAPTER 1
Introduction

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